Give or take a billion

You've had more experience with Dalmane (flurazepam HCI/Roche) than with any other benzodiazepine hypnotic...15 years' worth. You know you can *count* on it for sleep that satisfies patients—they fall asleep quickly and sleep through the night. 1-8 And the wide margin of safety with Dalmane⁷⁹ satisfies *you*. As always, caution patients about driving or drinking alcohol.



DALMARE flurazepam HCI/Roche ® sleep that satisfies

References: 1. Kales J, et al: Clin Pharmacol Ther 12:691-697, Jul-Aug 1971. 2. Kales A, et al: Clin Pharmacol Ther 18:356-363, Sep 1975. 3. Kales A, et al: Clin Pharmacol Ther 19:576-583, May 1976. 4. Kales A, et al: Clin Pharmacol Ther 19:576-583, May 1976. 4. Kales A, et al: Clin Pharmacol Ther 32:781-788, Dec 1982. 5. Frost JD Jr, DeLucchi MR: J Am Geriatr Soc 27:541-546, Dec 1979. 6. Dement WC, et al: Behav Med, pp. 25-31, Oct 1978. 7. Kales A, Kales JD: J Clin Psychopharmacol 3:140-150, Apr 1983. 8. Tennant FS, et al: Symposium on the Treatment of Sleep Disorders, Teleconference, Oct 16, 1984. 9. Greenblatt DJ, Allen MD, Shader RI: Clin Pharmacol Ther 21:355-361, Mar 1977.

DALMANE®

brand of

flurazepam HCI/Roche @ sleep that satisfies

15-mg/30-mg capsules

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; in acute or chronic medical situations requiring restful sleep. Objective sleep laboratory data have shown effectiveness for at least 28 consecutive nights of administration. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended. Repeated therapy should only be undertaken with appropriate patient evaluation.

Contraindications: Known hypersensitivity to flurazepam HCI; pregnancy, Benzodiazepines may cause fetal damage when administered during pregnancy. Several studies suggest an increased risk of congenital malformations associated with benzodiazepine use during the first trimester. Warn patients of the potential risks to the fetus should the possibility of becoming pregnant exist while receiving flurazepam. Instruct patients to discontinue drug prior to becoming pregnant. Consider the possibility of pregnancy prior to instituting therapy.

Warnings: Caution patients about possible combined

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. An additive effect may occur if alcohol is consumed the day following use for nightlime sedation. This potential may exist for several days following discontinuation. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Potential impairment of performance of such activities may occur the day following ingestion. Not recommended for use in persons under 15 years of age. Withdrawal symptoms rarely reported; abrupt discontinuation should be avoided with gradual tapering of dosage for those patients on medication for a prolonged period of time. Use caution in administering to addiction-prone individuals or those who might increase

Precautions: In elderly and debilitated patients, it is recommended that the dosage be limited to 15 mg to reduce risk of oversedation, dizziness, confusion and/or ataxia. Consider potential additive effects with other hypnotics or CNS depressents. Employ usual precautions in severely depressed patients, or in those with latent depression or suicidal tendencies, or in those with impaired renal or heparatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, porticularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and como, probably indicative of drug infolerance or overdosage, have been reported. Also reported: headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, Gl pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and Gu complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burring eyes, faintness, hypotension, shortness of breath, puritius, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, sturred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins, and alkaline phosphatase; and paradoxical reactions, e.g., excitement, stimulation and hyperactivity.

Dosage: Individualize for maximum beneficial effect.

Adults: 30 mg usual dosage; 15 mg may suffice in some patients. Elderly or debilitated patients: 15 mg recommended initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCI.



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THE ACE INHIBITOR HEART FAILURE

GIVE THE GIFT OF MORE ACTIVE LIVING



CAPOTEN ENHANCES PATIENTS' QUALITY OF LIFE

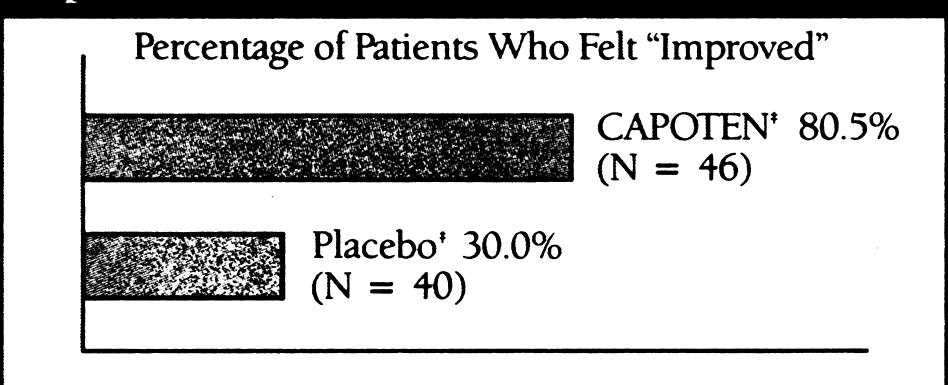
Relieves symptoms.

Significantly greater improvement in dyspnea, fatigue, orthopnea, and edema with CAPOTEN than with digitalis and diuretics alone.^{†1}

□ Increases ability to exercise.

A 24.3% increase after 12 weeks of CAPOTEN versus 0.4% with digitalis and diuretics alone.*1

8 out of 10 Patients Rated Themselves "Improved" with CAPOTEN



Use CAPOTEN when symptoms persist despite digitalis and diuretic therapy.

ACE THIBITOR ACE THIBITOR APOTEN FAILURES (captopril tablets)

YOUR FIRST CHOICE AFTER DIGITALIS AND DIURETICS

- *Angiotensin Converting Enzyme
- [†]Ninety-two patients, refractory to but continuing on digitalis and diuretics, were given CAPOTEN or placebo for 12 weeks. Patients were primarily New York Heart Association Class II and Class III. Dosages of CAPOTEN ranged from an initial 25 mg tid to a maximum maintenance dosage of 100 mg tid.
- ‡Given with digitalis and diuretics.
- SCAPOTEN is indicated in patients with heart failure who have not a sponded adequately to or cannot be controlled by conventional diuretic and digitalis therapy. CAPOTEN is to be used with diuretics and digitalis. In using CAPOTEN, consideration should be given to the risk of teletropenia agranulocytosis: Use special

INDICATIONS: Hypertension — CAPOTEN (captopril) is indicated for the treatment of hypertension. Consideration should be given to the risk of neutropenia/agranulocytosis (see WARNINGS). CAPOTEN may be used as initial therapy for patients with normal renal function, in whom the risk is relatively low. In patients with impaired renal function, particularly those with collagen vascular disease, captopril should be reserved for those who have either developed unacceptable side effects on other drugs, or have failed to respond satisfactorily to drug combinations. CAPOTEN is effective alone and in combination with other antihypertensive agents, especially thiazide-type diuretics.

Heart Failure: CAPOTEN (captopril) is indicated in patients with heart failure who have not responded adequately to or cannot be controlled by conventional diuretic and digitalis therapy. CAPOTEN is to be used with diuretics and digitalis.

WARNINGS: Neutropenia/Agranulocytosis — Neutropenia (< 1000/mm³) with myeloid hypoplasia has resulted from use of captopril. About half of the neutropenic patients developed systemic or oral cavity infections or other features of the syndrome of agranulocytosis. The risk of neutropenia is dependent on the clinical status of the patient:

In clinical trials in patients with hypertension who have normal renal function (serum creatinine < 1.6 mg/dL and no collagen vascular disease), neutropenia has been seen in one patient out of over 8,600 exposed. In patients with some degree of renal failure (serum creatinine at least 1.6 mg/dL) but no collagen vascular disease, the risk in clinical trials was about 1 per 500. Doses were relatively high in these patients, particularly in view of their diminished renal function. In patients with collagen vascular diseases (e.g., systemic lupus erythematosus, scleroderma) and impaired renal function, neutropenia occurred in 3.7% of patients in clinical trials. While none of the over 750 patients in formal clinical trials of heart failure developed neutropenia, it has occurred during subsequent clinical experience. Of reported cases, about half had serum creatinine ≥ 1.6 mg/dL and more than 75% received procainamide. In heart failure, it appears that the same risk factors for neutropenia are present.

Neutropenia has appeared usually within 3 months after starting therapy, associated with myeloid hypoplasia and frequently accompanied by erythroid hypoplasia and decreased numbers of megakaryocytes (e.g., hypoplastic bone marrow and pancytopenia); anemia and thrombocytopenia were sometimes seen. Neutrophils generally returned to normal in about 2 weeks after captopril was discontinued, and serious infections were limited to clinically complex patients. About 13% of the cases of neutropenia have ended fatally, but almost all fatalities were in patients with serious illness, having collagen vascular disease, renal failure, heart failure or immunosuppressant therapy, or a combination of these complicating factors.

Evaluation of the hypertensive or heart failure patient should always include assessment of renal function. If captopril is used in patients with impaired renal function, white blood cell and differential counts should be evaluated prior to starting treatment and at approximately 2-week intervals for about 3 months, then periodically. In patients with collagen vascular disease or who are exposed to other drugs known to affect the white cells or immune response, particularly when there is impaired renal function, captopril should be used only after an assessment of benefit and risk, and then with caution. All patients treated with captopril should be told to report any signs of infection (e.g., sore throat, fever); if infection is suspected, perform counts without delay. Since discontinuation of captopril and other drugs has generally led to prompt return of the white count to normal, upon confirmation of neutropenia (neutrophil count <1000/mm³) withdraw captopril and closely follow the patient's course.

Proteinuria — Total urinary proteins >1 g/day were seen in about 0.7% of patients on captopril. About 90% of affected patients had evidence of prior renal disease or received high doses (>150 mg/day), or both. The nephrotic syndrome occurred in about one-fifth of proteinuric patients. In most cases, proteinuria subsided or cleared within 6 months whether or not captopril was continued. The BUN and creatinine were seldom altered in proteinuric patients. Since most cases of proteinuria occurred by the 8th month of therapy, patients with prior renal disease or those receiving captopril at doses >150 mg/day should have urinary protein estimates (dip-stick on lst morning urine) before therapy, and periodically thereafter.

Hypotension — Excessive hypotension was rarely seen in hypertensive patients but is a possibility in severely salt/volume-depleted persons such as those treated vigorously with diuretics (see PRECAUTIONS [Drug Interactions]).

In heart failure, where blood pressure was either normal or low, transient decreases in mean blood pressure >20% were recorded in about half of the patients. This transient hypotension may occur after any of the first several doses and is usually well tolerated, although rarely it has been associated with arrhythmia or conduction defects. A starting dose of 6.25 or 12.5 mg tid may minimize the hypotensive effect. Patients should be followed closely for the first 2 weeks of treatment and whenever the dose of captopril and/or diuretic is increased.

BECAUSE OF THE POTENTIAL FALL IN BLOOD PRESSURE IN THESE PATIENTS, THERAPY SHOULD BE STARTED UNDER VERY CLOSE MEDICAL SUPERVISION.

PRECAUTIONS: General: Impaired Renal Function, Hypertension—Some hypertensive patients with renal disease, particularly those with severe renal artery stenosis, have developed increases in BUN and serum creatinine. It may be necessary to reduce captopril dosage and/or discontinue diuretic. For some of these patients, normalization of blood pressure and maintenance of adequate renal perfusion may not be possible. Heart Failure—About 20% of patients develop stable elevations of BUN and serum creatinine >20% above normal or baseline upon long-term treatment. Less than 5% of patients, generally with severe preexisting renal disease, required discontinuation due to progressively increasing creatinine. See DOSAGE AND ADMINISTRATION, ADVERSE REACTIONS (Altered Laboratory Findings). Valvular Stenosis—A theoretical concern, for risk of decreased coronary perfusion, has been noted regarding vasodilator treatment in patients with aortic stenosis due to decreased afterload reduction.

Surgery/Anesthesia — If hypotension occurs during major surgery or anesthesia, and is considered due to the effects of captopril, it is correctable by volume expansion.

Drug Interactions: Hypotension: Patients on Diuretic Therapy—Precipitous reduction of blood pressure may occasionally occur within the 1st hour after administration of the initial captopril dose in patients on diuretics, especially those recently placed on diuretics, and those on severe dietary salt restriction or dialysis. This possibility can be minimized by either discontinuing the diuretic or increasing the salt intake about 1 week prior to initiation of captopril therapy or by initiating therapy with small doses (6.25 or 12.5 mg). Alternatively, provide medical supervision for at least 1 hour after the initial dose.

Agents Having Vasodilator Activity - In heart failure patients, vasodilators should be administered with caution.

Agents Causing Renin Release — Captopril's effect will be augmented by antihypertensive agents that cause renin release.

Agents Affecting Sympathetic Activity — The sympathetic nervous system may be especially important in supporting blood pressure in patients receiving captopril alone or with diuretics. Beta-adrenergic blocking drugs add some further antihypertensive effect to captopril, but the overall response is less than additive. Therefore, use agents affecting sympathetic activity (e.g., ganglionic blocking agents or adrenergic neuron blocking agents) with caution.

Agents Increasing Serum Potassium—Give potassium-sparing diuretics or potassium supplements only for documented hypokalemia, and then with caution, since they may lead to a significant increase of serum potassium. Use potassium-containing salt substitutes with caution.

Inhibitors of Endogenous Prostaglandin Synthesis – Indomethacin and other nonsteroidal anti-inflammatory agents may reduce the antihypertensive effect of captopril, especially in low renin hypertension.

Drug/Laboratory Test Interaction: Captopril may cause a false-positive urine test for acetone.

Carcinogenesis, Mutagenesis and Impairment of Fertility: Two-year studies with doses of 50 to 1350 mg/kg/day in mice and rats failed to show any evidence of carcinogenic potential. Studies in rats have revealed no impairment of fertility.

Pregnancy: Category C—There are no adequate and well-controlled studies in pregnant women. Embryocidal effects and craniofacial malformations were observed in rabbits. Therefore, captopril should be used during pregnancy, or for patients likely to become pregnant, only if the potential benefit outweighs the potential risk to the fetus. Captopril crosses the human placenta.

Nursing Mothers: Captopril is secreted in human milk. Exercise caution when administering captopril to a nursing woman, and, in general, nursing should be interrupted.

Pediatric Use: Safety and effectiveness in children have not been established

Pediatric Use: Safety and effectiveness in children have not been established although there is limited experience with use of captopril in children from 2 months to 15 years of age. Dosage, on a weight basis, was comparable to that used in adults. Captopril should be used in children only if other measures for controlling blood pressure have not been effective.

ADVERSE REACTIONS: Reported incidences are based on clinical trials involving approximately 7000 patients.

Renal — About 1 of 100 patients developed proteinuria (see WARNINGS). Renal insufficiency, renal failure, polyuria, oliguria, and urinary frequency in 1 to 2 of 1000 patients.

Hematologic – Neutropenia/agranulocytosis have occurred (see WARNINGS). Anemia, thrombocytopenia, and pancytopenia have been reported.

Dermatologic — Rash (usually maculopapular, rarely urticarial), often with pruritus and sometimes with fever and eosinophilia, in about 4 to 7 of 100 patients (depending on renal status and dose), usually during the 1st 4 weeks of therapy. Pruritus, without rash, in about 2 of 100 patients. A reversible associated pemphigoid-like lesion, and photosensitivity have also been reported. Angioedema of the face, mucous membranes of the mouth, or of the extremities in about 1 of 1000 patients—reversible on discontinuance of captopril therapy. One case of laryngeal edema reported. Flushing or pallor in 2 to 5 of 1000 patients.

Cardiovascular — Hypotension may occur, see WARNINGS and PRECAUTIONS (Drug Interactions) for discussion of hypotension on initiation of captopril therapy. Tachycardia, chest pain, and palpitations each in about 1 of 100 patients. Angina pectoris, myocardial infarction, Raynaud's syndrome, and congestive heart failure each in 2 to 3 of 1000 patients.

Dysgeusia — About 2 to 4 (depending on renal status and dose) of 100 patients developed a diminution or loss of taste perception; taste impairment is reversible and usually self-limited even with continued drug use (2 to 3 months). Gastric irritation, abdominal pain, nausea, vomiting, diarrhea, anorexia, constipation, aphthous ulcers, peptic ulcer, dizziness, headache, malaise, fatigue, insomnia, dry mouth, dyspnea, cough, alopecia, and paresthesias reported in about 0.5 to 2% of patients but did not appear at increased frequency compared to placebo or other treatments used in controlled trials.

Altered Laboratory Findings: Elevations of liver enzymes in a few patients although no causal relationship has been established. Rarely cholestatic jaundice and hepatocellular injury with or without secondary cholestasis, have been reported. A transient elevation of BUN and serum creatinine may occur, especially in volume-depleted or renovascular hypertensive patients. In instances of rapid reduction of longstanding or severely elevated blood pressure, the glomerular filtration rate may decrease transiently, also resulting in transient rises in serum creatinine and BUN. Small increases in serum potassium concentration frequently occur, especially in patients with renal impairment (see PRECAUTIONS).

OVERDOSAGE: Primary concern is correction of hypotension. Volume expansion with an I.V. infusion of normal saline is the treatment of choice for restoration of blood pressure. Captopril may be removed from the general circulation by hemodialysis.

DOSAGE AND ADMINISTRATION: CAPOTEN (captopril) should be taken one hour before meals. In hypertension, CAPOTEN may be dosed bid or tid. Dosage must be individualized; see DOSAGE AND ADMINISTRATION section of package insert for detailed information regarding dosage in hypertension and in heart failure. Because CAPOTEN (captopril) is excreted primarily by the kidneys, dosage adjustments are recommended for patients with impaired renal function.

Consult package insert before prescribing CAPOTEN (captopril).

HOW SUPPLIED: Available in tablets of 12.5, 25, 50, and 100 mg in bottles of 100 (25 mg also available in bottles of 1000), and in UNIMATIC* single dose packs of 100 tablets. (J3-658D)

Reference: 1. Cannon PJ, Criley JM, Dzau VJ, et al: A placebo-controlled trial of captopril in refractory chronic congestive heart failure. J Am Col Cardiol 2:755–763, 1983.



INNOVATORS IN CARDIOVASCULAR MEDICINE



(metaproterenol sulfate)

Bronchodilator

Medi-Cal Number: 1031F-CC

Up to six hours of bronchodilator efficacy

Accuracy and convenience in a single vial

No metabisulfites

Alupent® (metaproterenol sulfate)

Inhalant Solution Unit-Dose Vial Bronchodilator

Brief Summary of Prescribing Information

INDICATIONS AND USAGE Alupent[®] (metaproterenol sulfate) Inhalant Solution is indicated as bronchodilator for bronchial asthma and for reversible bronchospasm which may occur in association with bronchitis and emphysema.

CONTRAINDICATIONS Use in patients with cardiac arrhythmias associated with tachycardia is contraindicated.

Although rare, immediate hypersensitivity reactions can occur. Therefore, Alupent (metaproterenol sulfate) Inhalant Solution, 0.6% is contraindicated in patients with a history of hypersensitivity to any of its components.

WARNINGS Excessive use of adrenergic aerosols is potentially dangerous. Fatalities have been reported following excessive use of Alupent (metaproterenol sulfate) as with other sympathomimetic inhalation preparations, and the exact cause is unknown. Cardiac arrest was noted in coveral cases.

Paradoxical bronchoconstriction with repeated excessive administration has been noted with sympathomimetic agents.

Patients should be advised to contact their physician in the event that they do not respond to their usual dose of sympathomimetic amine aerosol.

PRECAUTIONS Because Alupent (metaproterenol sulfate) Inhalant Solution is a sympathomimetic drug, it should be used with great caution in patients with hypertension, coronary artery disease, congestive heart failure, hyperthyroidism or diabetes, or when there is sensitivity to sympahomimetic amines.

nformation for Patients Extreme care must be exercised with respect to he administration of additional sympathomimetic agents. A sufficient nterval of time should elapse prior to administration of another sympathomimetic agent.

Parcinogenesis Long-term studies in mice and rats to evaluate the oral carcinogenic potential of metaproterenol sulfate have not been completed. Studies of metaproterenol sulfate have not been conducted to determine nutagenic potential or effect on fertility.

'regnancy Teratogenic Effects: Pregnancy Category C. Alupent (meta-

proterenol sulfate) has been shown to be teratogenic and embryocidal in rabbits when given orally in doses 620 times the human inhalation dose. There are no adequate and well-controlled studies in pregnant women. Alupent should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Oral reproduction studies in mice, rats and rabbits showed no teratogenic or embryocidal effects at 50 mg/kg corresponding to 310 times the human inhalation dose. Teratogenic effects in the rabbit included skeletal abnormalities and hydrocephalus with bone separation.

Nursing Mothers It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk. caution should be exercised when Alupent (metaproterenol sulfate) is administered to a nursing woman.

Pediatric Use Safety and effectiveness in children below the age of 12 have not been established.

ADVERSE REACTIONS Adverse reactions are similar to those noted with other sympathomimetic agents.

The most frequent adverse reactions to Alupent (metaproterenol sulfate) are nervousness and tachycardia which occur in about 1 in 7 patients. tremor which occurs in about 1 to 20 patients and nausea which occurs in about 1 in 50 patients. Less frequent adverse reactions are hypertension palpitations, vomiting and bad taste which occur in approximately 1 in 300 patients.

HOW SUPPLIED Alupent (metaproterenol sulfate) Inhalant Solution Unit Dose Vials are supplied as 0.6% clear colorless or nearly colorless solution, each vial containing 2.5 ml, with 25 vials per box. Do not use the solution if it is brown or has a precipitate.

Consult package insert before prescribing.

AL-UD-BPI-5/86



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The Only Nicroencapsulated KCl Delivery System That Delivers Both 8mEq K& 10mEq K



MCRO-K MICRO-K'10

(Potassium Chloride)

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(Potassium Chloride)

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CORGARI (nadolol tablets)

Preserves renal blood flow



CORGARD® TABLETS

DESCRIPTION: CORGARD (nadolol) is a synthetic non-selective beta-adrenergic receptor

CONTRAINDICATIONS: Bronchial asthma, sinus bradycardia and greater than first degree conduction block, cardiogenic shock, and overt cardiac failure (see WARNINGS).

WARNINGS: Cardiac Failure—Sympathetic stimulation may be a vital component supporting circulatory function in congestive heart failure, and its inhibition by beta-blockade may precipi tate more severe failure. Although beta-blockers should be avoided in overt congestive heart failure, if necessary, they can be used with caution in patients with a history of failure who are well-compensated, usually with digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle. IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta-blockers can, in some cases, lead to cardiac failure; therefore, at first sign or symptom of heart failure, digitalize and/or give diuretics, and closely observe response, or discontinue nadolol (gradually if possible).

Exacerbation of Ischemic Heart Disease Following Abrupt Withdrawal-Hypersensitivity to catecholamines has been observed in patients withdrawn from beta-blocker therapy; exacerbation of angina and, in some cases, myocardial infarction have occurred after abrupt discontinuation of such therapy. When discontinuing chronic use of nadolol, particularly in patients with ischemic heart disease, gradually reduce dosage over a 1- to 2- week period and carefully monitor the patient. Reinstitute nadolol promptly (at least temporarily) and take other measures appropriate for management of unstable angina if angina markedly worsens or acute coronary insufficiency develops. Warn patients not to interrupt or discontinue therapy without physician's advice. Because coronary artery disease is common and may be unrecognized, it may be prudent not to discontinue nadolol therapy abruptly even in patients treated only for hypertension.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema)—PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA-BLOCKERS. Administer nadolol with caution since it may block bronchodilation produced by endogenous or exogenous catecholamine stimulation of beta2 receptors.

Major Surgery—Because beta blockade impairs the ability of the heart to respond to reflex stimuli and may increase risks of general anesthesia and surgical procedures, resulting in protracted hypotension or low cardiac output, it has generally been suggested that such therapy should be withdrawn several days prior to surgery. Recognition of the increased sensitivity to catecholamines of patients recently withdrawn from beta-blocker therapy, however, has made this recommendation controversial. If possible, withdraw beta-blockers well before surgery takes place. In emergency surgery, inform the anesthesiologist that the patient is on betablocker therapy. Use of beta-receptor agonists such as isoproterenol, dopamine, dobutamine, or levarterenol can reverse the effects of nadolol. Difficulty in restarting and maintaining the heart beat has also been reported with beta-adrenergic receptor blocking agents.

es and Hypoglycemia-Beta-adrenergic blockade may prevent the appearance of premonitory signs and symptoms (e.g., tachycardia and blood pressure changes) of acute hypoglycemia. This is especially important with labile diabetics. Beta-blockade also reduces release of insulin in response to hyperglycemia; therefore, it may be necessary to adjust dose of antidiabetic drugs.

 Beta-adrenergic blockade may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. To avoid abrupt withdrawal of beta-adrenergic blockade which might precipitate a thyroid storm, carefully manage patients suspected of developing thyrotoxicosis. PRECAUTIONS: Impaired Renal Function—Use nadolol with caution (see DOSAGE AND ADMINISTRATION section of package insert).

Information for Patients—Warn patients, especially those with evidence of coronary artery

insufficiency, against interruption or discontinuation of nadolol without physician's advice. Although cardiac failure rarely occurs in properly selected patients, advise patients being treated with beta-adrenergic blocking agents to consult physician at first sign of impending failure. Advise patients in event of missed doses.

Drug Interactions—Concurrent administration may result in interactions with: Anesthetics. general-exaggeration of the hypotension induced by general anesthetics (see WARNINGS, Major Surgery). Antidiabetic drugs (oral agents and insulin)—hypoglycemia or hyperglycemia; adjust antidiabetic drug dosage accordingly (see WARNINGS, Diabetes and Hypoglycemia). Catecholamine-depleting drugs (e.g., reserpine)—additive effect; monitor closely for hypotension and/or excessive bradycardia.

Carcinogenesis, Mutagenesis, Impairment of Fertility-In 1 to 2 years oral toxicologic studies in mice, rats, and dogs, nadolol did not produce significant toxic effects. In 2-year oral carcinogenic studies in rats and mice, nadolol did not produce neoplastic, preneoplastic, or nonneoplastic pathologic lesions.

Pregnancy Category C—In animal reproduction studies with nadolol, evidence of embryo-and fetotoxicity was found in rabbits (but not in rats or hamsters) at doses 5 to 10 times greater (on a mg/kg basis) than maximum indicated human dose; no teratogenic potential was seen in any of these species. There are no well-controlled studies in pregnant women; therefore, use nadolol in pregnant women only if potential benefit justifies potential risk to the fetus. Neonates of mothers who received nadolol at parturition have exhibited bradycardia, hypoglycemia and associated symptoms.

Nursing Mothers-Nadolol is excreted in human milk. Exercise caution when nadolol is red to a nursing woman

Pediatric Use-Safety and effectiveness in children have not been established

ADVERSE REACTIONS: Most adverse effects have been mild and transient and have rarely required nadolol withdrawal.

Cardiovascular-Bradycardia with heart rates of less than 60 beats per minute occurs commonly, and heart rates below 40 beats per minute and/or symptomatic bradycardia were seen in about 2 of 100 patients. Symptoms of peripheral vascular insufficiency, usually of the Raynaud type, have occurred in approximately 2 of 100 patients. Cardiac failure, hypotension, and rhythm/conduction disturbances have each occurred in about 1 of 100 patients. Single instances of first degree and third degree heart block have been reported; intensification of AV block is a known effect of beta-blockers (see also CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS). Central Nervous System—Dizziness or fatigue reported in approximately 2 of 100 patients; paresthesias, sedation, and change in behavior reported in approximately 6 of 1000 patients. Respiratory—Bronchospasm reported in approximately 1 of 1000 patients (see CONTRAINDICATIONS and WARNINGS). Gastrointestinal—Nausea, diarrhea, abdominal discomfort, constipation, vomiting, indigestion, anorexia, bloating, and flatulence each reported in 1 to 5 of 1000 patients. **Miscellaneous**—Each of the following reported in 1 to 5 of 1000 patients: rash; pruritus; headache; dry mouth, eyes, or skin; impotence or decreased libido; facial swelling; weight gain; slurred speech; cough; nasal stuffiness; sweating; tinnitus; blurred vision: infrequent reversible alopecia.

The following adverse reactions have been reported in patients taking nadolol and/or other beta-adrenergic blocking agents, but no causal relationship to nadolol has been established. **Central Nervous System**—reversible mental depression progressing to catatonia; visual disturbances; hallucinations; an acute reversible syndrome characterized by disorientation for time and place; short-term memory loss, emotional lability with slightly clouded sensorium; decreased performance on neuropsychometrics. Gastroint tinal-mesenteric arterial thrombosis; ischemic collitis; elevated liver enzymes. **Hematologic**—agranulocytosis; thrombocytopenic or nonthrombocytopenic or nonthrombocytopenic purpura. **Allergic**—lever combined with aching and sore throat; laryngospasm; respiratory distress. **Miscellaneous**—pemphigoid rash; hypertensive reaction in patients with pheochromocytoma; sleep disturbances; Peyronie's disease. The oculomucocutaneous syndrome associated with practolol has not been reported with nadolo

OVERDOSAGE: Nadolol can be removed from the general circulation by hemodialysis. In addition to gastric lavage, employ the following measures as appropriate. In determining duration of corrective therapy, take note of long duration of effect of nadolol.

Excessive Bradycardia—Administer atropine (0.25 to 1.0 mg). If there is no response to vagal blockade, administer isoproterenol cautiously.

Cardiac Failure-Administer a digitalis glycoside and diuretic. It has been reported that glucagon may also be useful in this situation. **Hypotension**—Administer vasopressors, e.g., epinephrine or levarterenol. (There is evidence

that epinephrine may be the drug of choice.)

Bronchospasm—Administer a beta₂-stimulating agent and/or a theophylline derivative.

DOSAGE—For all patients, DOSAGE MUST BE INDIVIDUALIZED.

For angina pectoris, usual initial dose is 40 mg q.d.; may be gradually increased in 40 to 80 mg increments at 3 to 7 day intervals until optimum clinical response or pronounced slowing of the heart rate; usual maintenance dose is 40 or 80 mg q.d. (doses up to 160 or 240 mg daily may be needed). If treatment is to be discontinued, reduce dosage gradually over a period of 1 to 2 weeks (see WARNINGS).

For hypertension, usual initial dose is 40 mg q.d.; gradually increase in 40 to 80 mg inc ments until optimum blood pressure reduction is achieved; usual maintenance dose is 40 or 80 mg q.d. (doses up to 240 or 320 mg daily may be needed).

Patients with renal failure require adjustment in dosing interval; see package insert for dosage in these patients.

For full prescribing information consult package insert.

HOW SUPPLIED: In scored tablets containing 40, 80, 120, or 160 mg nadolol per tablet in bottles of 100 and in Unimatic* unit-dose packs of 100 tablets. The 40 mg, 80 mg, and 120 mg potencies are also available in bottles of 1000 tablets.

References: 1. Alexander JC, Christie MH, Vernam KA, et al: Long-term experience with nadolol in treatment of hypertension and angina pectoris. Am Heart J 108:1136-1140, 1984.



IN THE HYPERTENSIVE PATIENT

(nadolol tablets)

PRESERVES REMAL BLOOD FLOW...

AN UNDERLYING PHARMACOLOGIC CONSIDERATION



By preserving renal blood flow, CORGARD can minimize the compensatory sodium and water retention which may aggravate hypertension.

In a 2-year study of 106 hypertensive patients treated with CORGARD, serum creatinine, an indicator of renal function, decreased 20% from baseline.¹

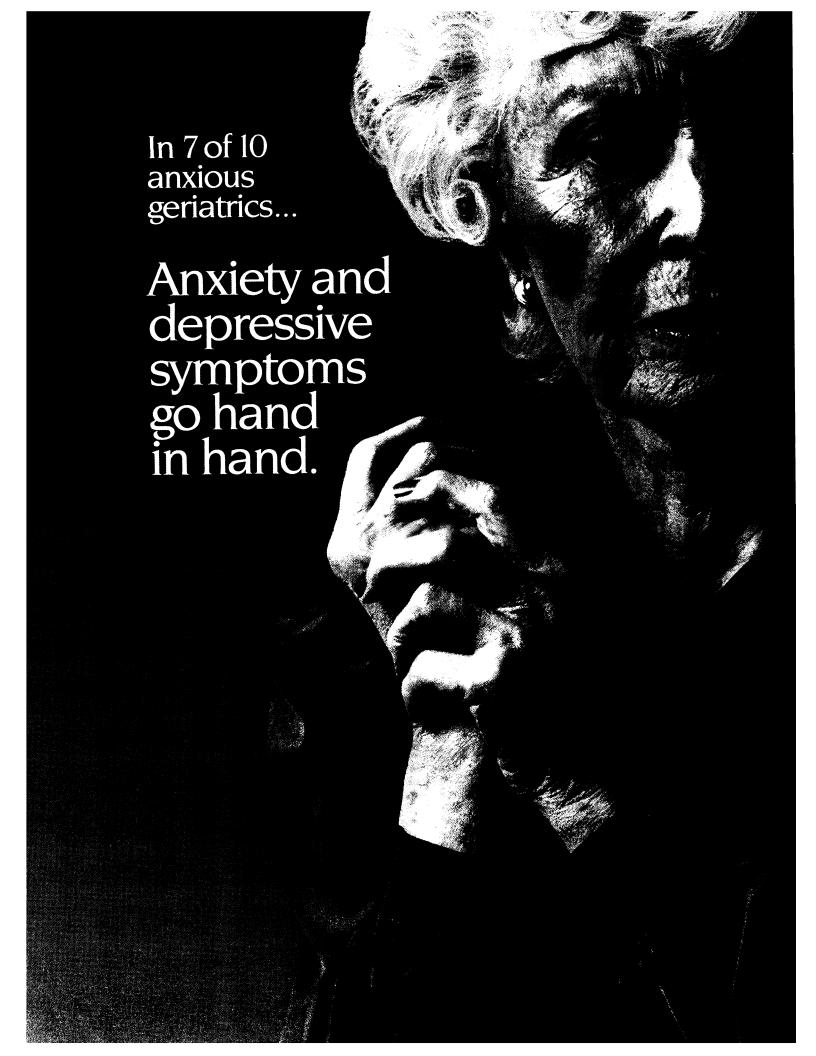




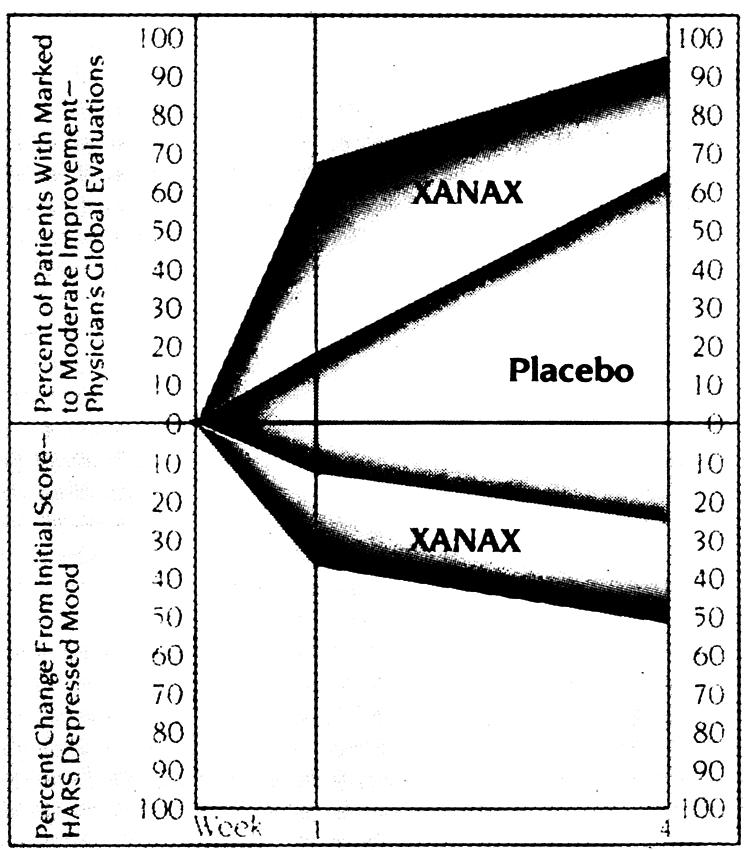
Aotrin 80 ibuprofen

Extra strength Convenience Economy





Xanax effectively relieves anxiety with associated depressive symptoms.



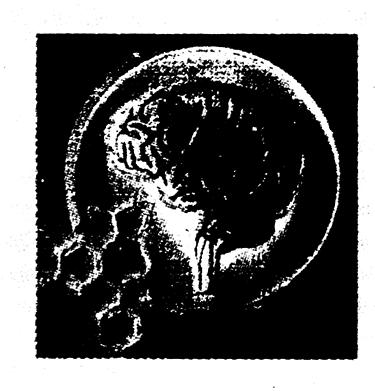
In a recent clinical study of 83 geriatric patients with clinical anxiety, 73% were diagnosed as having symptoms of depressed mood.

XANAX is well suited for therapy because it demonstrates greater efficacy than does placebo in reducing the Hamilton Anxiety Rating Scale Total Score and individual items, including depressed mood (see Figure).

advantages for genatic patients.

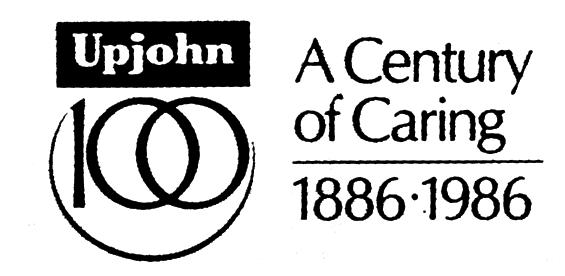
- Effectively relieves the symptoms of anxiety
- Also relieves anxiety with associated depressed mood
- Well tolerated—side effects, if they occur, are generally observed at the beginning of therapy and usually disappear with continued medication. Drowsiness and light-headedness were the most commonly reported adverse reactions
- Does not cause cardiovascular toxicity
- Specific geriatric dosage—0.25 mg, two or three times daily

I. Cohn JB: Double-blind safety and efficacy comparison of alprazolam and placebo in the treatment of anxiety in geriatric patients. Curr Ther Res 1984:35(1):100-112.



Alax 0.25 mg
Tablets

alprazolam ©



XANAX Tablets (alprazolam) @

CONTRAINDICATIONS

Patients with sensitivity to this drug or other benzodiazepines and in acute narrow angle glaucoma.

WARNINGS

Not of value in psychotic patients. Caution patients against hazardous occupations requiring complete mental alertness and about the simultaneous ingestion of alcohol and other CNS depressant drugs.

Benzodiazepines can cause fetal harm in pregnant women. Warn patients of the potential hazard to the fetus. Avoid during the first trimester.

PRECAUTIONS

General: The dosage of XANAX Tablets should be reduced or withdrawn gradually, since withdrawal seizures have been reported upon abrupt withdrawal. If XANAX is combined with other psychotropics or anticonvulsant drugs, consider drug potentiation (see Drug Interaction section). Exercise the usual precautions regarding size of the prescription for depressed or suicidal patients. In elderly and debilitated patients, use the lowest possible dosage (see Dosage and Administration). Observe the usual precautions in treating patients with impaired renal or hepatic function.

Information for Patients: Alert patients about: (a) consumption of alcohol and drugs. (b) possible fetal abnormalities. (c) operating machinery or driving, (d) not increasing dose of the drug due to risk of dependence, (e) not stopping the drug abruptly. Laboratory Tests: Not ordinarily required in otherwise healthy patients. Drug Interactions: Additive CNS depressant effects with other psychotropics, anticonvulsants, antihistamines, ethanol and other CNS depressants. Pharmacokinetic interactions with benzodiazepines have been reported. Drug/Laboratory Test Interactions: No consistent pattern for a specific drug or specific test. Carcinogenesis. Mulagenesis, Impairment of Fertility: No carcinogenic Effects: The child born of a mother on benzodiazepines may be at some risk for withdrawal symptoms and neonatal flaccidity. Labor and Delivery: No established use. Nursing Mothers: Benzodiazepines are excreted in human milk. Women on XANAX should not nurse. Pediatric Use: Safety and effectiveness in children below the age of 18 have not been established.

ADVERSE REACTIONS

Side effects are generally observed at the beginning of therapy and usually disappear with continued medication. In the usual patient, the most frequent side effects are likely to be an extension of the pharmacologic activity of XANAX, eg. drowsiness or lightheadedness.

Central nervous system. Drowsiness, lightheadedness, depression, headache, confusion, insomnia, nervousness, syncope, dizziness, akathisia, and tiredness/sleeniness

Gastrointestinal: Dry mouth, constipation, diarrhea, nausea/vomiting, and increased salivation.

Cardiovascular: Tachycardia/palpitations, and hypotension.

Sensory: Blurred vision.

Musculoskeletal: Rigidity and tremor.

Cutaneous: Dermatitis/allergy.

Other side effects: Nasal congestion, weight gain, and weight loss.

In addition, the following adverse events have been reported with the use of benzodiazepines: dystonia, irritability, concentration difficulties, anorexia, transient amnesia or memory impairment, loss of coordination, fatigue, sedation, slurred speech, jaundice, musculoskeletal weakness, pruritus, diplopia, dysarthria, changes in libido, menstrual irregularities, incontinence and urinary retention.

Paradoxical reactions such as stimulation, agitation, increased muscle spasticity, sleep disturbances, and hallucinations may occur. Should these occur, discontinue the drug.

During prolonged treatment, periodic blood counts, urinalysis, and blood chemistry analysis are advisable. Minor EEG changes of unknown significance have been observed

DRUG ABUSE AND DEPENDENCE

Physical and Psychological Dependence: Withdrawal symptoms have occurred following abrupt discontinuance of benzodiazepines. Withdrawal seizures have occurred upon rapid decrease or abrupt discontinuation of therapy. In all patients, dosage should be gradually tapered under close supervision. Patients with a history of seizures or epilepsy should not be abruptly withdrawn from XANAX. Addiction-prone individuals should be under careful surveillance. Controlled Substance Class: XANAX is a controlled substance and has been assigned to schedule IV.

DOSAGE AND ADMINISTRATION

The usual starting dose is 0.25 to 0.5 mg, t.i.d. Maximum total daily dose is 4 mg. In the elderly or debilitated, the usual starting dose is 0.25 mg, two or three times daily. Reduce dosage gradually when terminating therapy, by no more than one milligram every three days.

CAUTION: FEDERAL LAW PROHIBITS DISPENSING WITHOUT PRESCRIPTION.

B-4-



J-5963 January 1986

PHYSICIANS



The Air Force Reserve has a position for you!

With only one day a month, plus a twelve day annual tour of active duty participation, the Air Force Reserve can offer you the benefits that count! And, there's no relocation or interruption of your present practice with your Air Force Reserve association. For a change of pace, call or write the location listed below, providing your name, specialty, phone number, and address.

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AIR FORCE RESERVE

26-601-1702

A GREAT WAY TO SERVE



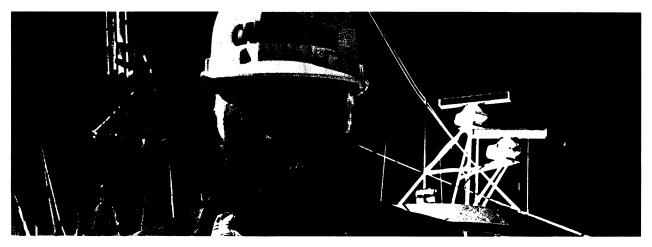
CARDIZEM: FEW SIDE EFFECTS

diltiazem HCI/Marion

- Antianginal action includes dilatation of coronary arteries, a decrease in vascular resistance/afterload, and a reduction in heart rate
- Proven efficacy when used alone in angina'
- Compatible with other antianginals 2,3*
- A safe choice for angina patients with coexisting hypertension, asthma, COPD, or PVD^{4,5}

*See Warnings and Precautions.

Please see brief summary of prescribing information on the next page.



CARDIZEM® FEW SIDE EFFECTS IN ANTIANGINAL THERAPY diltiazem HCI/Marion

60 mg tid or gid

Brief SummaryProfessional Use Information

CARDIZEM®

(diltiazem HCI) 30 mg and 60 mg Tablets

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacernaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic). WARNINGS

- Cardiac Conduction. CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularty in potients with sick sinus syndrome) or second- or third-degree AV block (six of 1,243 patients for 0,48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with print product against developed printing of a partial printing against a partial printing of a partial printing against a Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of
- Congestive Heart Failure. Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). Experience with the use of CARDIZEM alone or in combination with beta-blockers in

patients with impaired ventricular function is very

limited. Caution should be exercised when using the drug in such patients.
Hypotension. Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension. 3.

Acute Hepatic Injury. In rare instances, significant elevations in enzymes such as alkaline phosphatase, CPK, LDH, SGOT, SGPT, and other symptoms consistent with acute hepatic injury have been noted. These reactions have been reversible upon dispositionation of dent there as The satellarsain. discontinuation of drug therapy. The relationship to CARDIZEM is uncertain in most cases, but prob-able in some. (See PRECAUTIONS.)

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic

function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of dilliazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these

associated with hepatic changes; however, these changes were reversible with continued dosing. **Drug Interaction.** Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS.)

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular. treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diffiazem has been shown to increase

serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of

Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial

tests. No intrinsic effect on fertility was observed in rats. **Pregnancy.** Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the

Nursina Mothers. Diltiazem is excreted in human milk. One report suggests that concentrations in breas. milk may approximate serum levels. If use of CARDIZEM is deemed essential, an alternative method of infant

reeding should be instituted.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac

conduction abnormalities have usually been excluded. In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy. The following represent occurrences observed in clinical studies which can be at least reasonably asso-

ciated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences as well as their frequency of presentation are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%). In addition, the following events were reported infrequently (less than 1%): Angina, arrhythmia, AV block (first Cardiovascular:

Augura, armynimia, Av block (instance), AV block (second or third degree — see conduction warming), bradycardia, congestive heart failure, flushing, hypotension, palpitistics, process

tations, syncope. Amnesia, gait abnormality, halluci-nations, insomnia, nervousness,

Nervous System:

paresthesia, personality change, somnolence, tinnitus, tremor. Gastrointestinal: Anorexia, constipation, diarrhea,

dysgeusia, dyspepsia, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH (see hepatic

warnings), vomiting, weight

Dermatologic. Petechiae, pruritus, photosensitivity, urticaria.

Other:

Amblyopia, dyspnea, epistaxis, eye irritation, hyperglycemia, nasal congestion, nocturia, osteoarticular pain, polyuria, sexual difficulties

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: reported intrequently in patients receiving CARLINEAM, alopecia, gingival hyperplasia, erythema multiforme, and leukopenia. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

ISSUED 7/86 established. Issu See complete Professional Use Information before

prescribing.

References: 1. Pepine C.J. Feldman RL, Hill JA, et al: Clinical outcome after treatment of rest angina with calcium blockers: Comparative experience during the initial year of therapy with dittiazem, nifedipine, and verapamil. <u>Am Heart J</u> 1983, 106(6): 1341-1347. **2.** Shapiro W: Calcium channel blockers: Actions on the heart and uses in ischemic heart disease. <u>Consultant</u> 1984;24(Dec): 150-159. **3.** Johnston DL, Lesoway R, Humen DP, et al. Clinical and hemodynamic evaluation of propranolol in combination with verapamil, nifedipine and diltiazem in exertional angina pectoris: A placebocontrolled, double-blind, randomized, crossover study.

Am J Cardiol 1985;55:680-687. 4. Cohn PF, Braunwald E: Chronic ischemic hand disease. E Chronic ischemic heart disease, in Braunwald E (ed): Heart Disease: A Textbook of Cardiovascular Medicine, ed 2. Philadelphia, WB Saunders Co, 1984, chap 39. Schroeder JS: Calcium and beta blockers in ischemic heart disease: When to use which. <u>Mod Med</u> 1982;50(Sept):94-116.

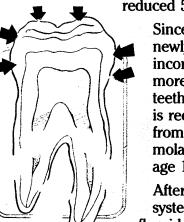






Dental Caries Can Be Reduced 50-80%

Developing primary and permanent teeth supplied with systemic fluoride are so much stronger that later caries can be reduced 50-80%.¹²



Since pre-eruptive and newly erupted teeth incorporate fluoride more easily than older teeth, systemic fluoride is required every day-from birth until final molars appear (around age 13).

After teeth appear, systemic and topical fluoride work together

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Vi-Flor® Vitamin/ Fluoride Combination Enhances Compliance

Daily vitamins already containing fluoride make compliance easy and economical for parents.

Regular fluoride updates in the office remind parents of the importance of daily systemic fluoride.



fluoride vitamins.See attached statement for full prescribing information.





REFERENCES:

Assenden R and Peebles T: Effects of Fluoride Supplementation From Birth on Human Deciduous and Permanent Teeth. Arch. Oral. Biol. 19321, 1974.
Hambert 1: Controlled Trial of Phonide in Vitamin Drons for Prevention of Caries in

Chiarnen, Langest ren. 27, 1971, p. 342.
Newbrum, E.: How Fhoroide Works: Topical vs. Systemic Action, in Mead Johnson Clinical
Report Series, Clinical Importance of Pluoride Nutrition in Infants, Children and Young
Adults, Chicago, Pragmatum 1 1985, a
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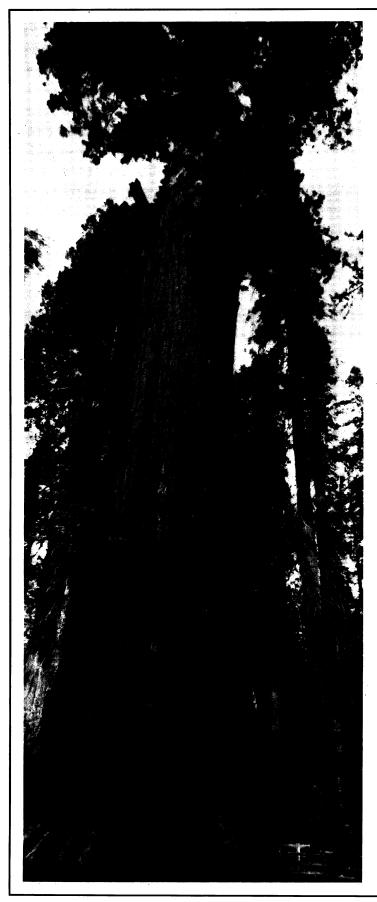




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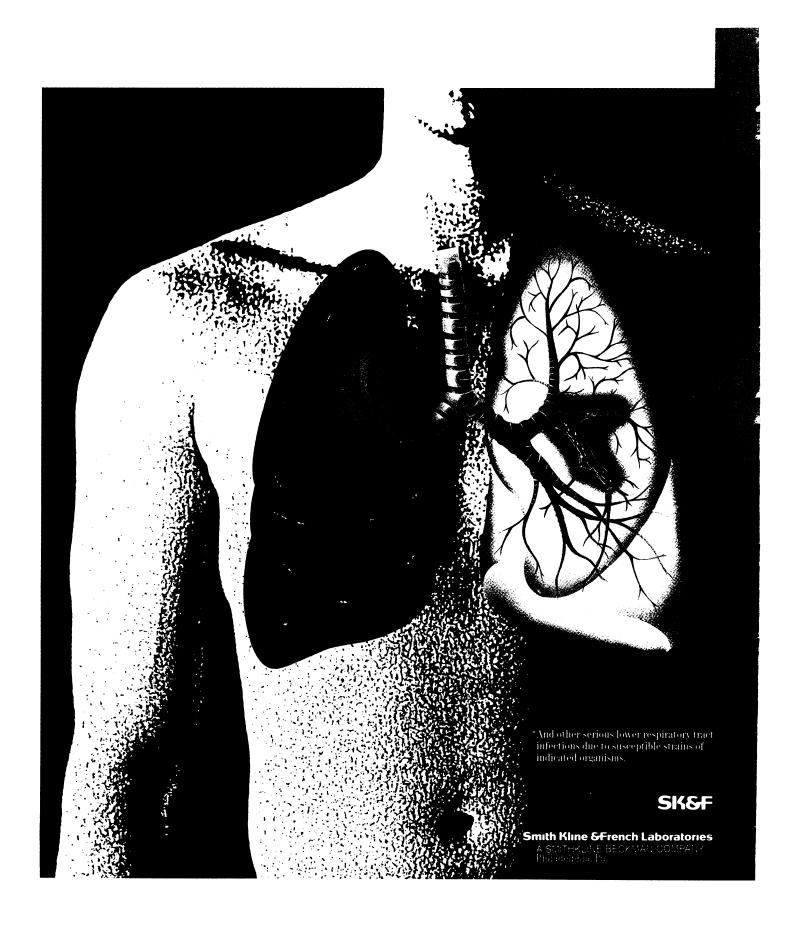
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In Pneumonia*... The



'Monocid' Advantage

- 24-Hour Coverage of Common Pathogens
- Effective Against Ampicillin-Resistant *H. influenzae*
- I.V. or I.M.: Hospital or Outpatient Management
- Lowest Cost per Course of Therapy¹⁻⁴

• 95% Clinical Success (91% cured,* 4% improved) with Once-Daily Dosing⁵⁻⁷

Once-a-Day/Broad-Spectrum

ACONOCID® brand of sterile Cefonicid sodium

Cefonicid sodium (lyophilized)

^{*}Since the definition of "cure" may vary significantly among clinical settings and investigators, the reader is urged to consult the references cited.

Before prescribing, please consult the brief summary of 'Monocid' prescribing information on the following page.



cefonicid sodium (lyophilized)

Before prescribing, see complete prescribing information in SK&F literature or PDR. The following is a brief summary.

INDICATIONS AND USAGE

Monocid (sterile cefonicid sodium, SK&F) is indicated in the treatment of infections due to susceptible strains of the microorganisms listed below:

LOWER RESPIRATORY TRACT INFECTIONS, due to Streptococcus pneumoniae (formerly D. pneumoniae); Klebsiella pneumoniae; Escherichia coli; and Hemophilus influenzae (ampicillin-resistant and ampicillin-sensitive).

URINARY TRACT INFECTIONS, due to Escherichia coli; Proteus mirabilis (indolenegative Proteus); and Klebsiella pneumoniae.

SKIN AND SKIN STRUCTURE INFECTIONS, due to Staphylococcus aureus and S. epidermidis; Streptococcus pyogenes (Group A Streptococcus) and S. agalactiae (Group B Streptococcus).

SEPTICEMIA, due to Streptococcus pneumoniae (formerly D. pneumoniae) and

BONE AND JOINT INFECTIONS, due to Staphylococcus aureus.

Therapy with 'Monocid' may be initiated pending results of susceptibility studies. Treatment should be adjusted according to findings.

SURGICAL PROPHYLAXIS

SURGICAL PROPHYLAXIS

Administration of a single 1 gram dose of 'Monocid' before surgery may reduce the incidence of postoperative infections in patients undergoing surgical procedures classified as contaminated or potentially contaminated (e.g., colorectal surgery, vaginal hysterectomy, or cholecystectomy in high-risk patients), or in patients in whom infection at the operative site would present a serious risk (e.g., prosthetic arthroplasty, open heart surgery). Although cefonicid has been shown to be as effective as cefazolin in prevention of infection following coronary artery bypass surgery, no placebo-controlled trials have been conducted to evaluate any cephalosporin antibiotic in the prevention of infection following coronary artery bypass surgery or prosthetic heart valve replacement.

In cesarean section, the use of 'Monocid' (after the umbilical cord has been clamped) may reduce the incidence of certain postoperative infections.

When administered one hour prior to surgical procedures for which it is indicated, a single 1 gram dose of 'Monocid' provides protection from most infections due to susceptible organisms throughout the course of the procedure and for approximately 24 hours after administration. Intraoperative and postoperative administration of 'Monocid' is not necessary. Daily doses of 'Monocid' may be administered for two additional days in patients undergoing prosthetic arthroplasty or open heart surgery. Before using 'Monocid' concomitantly with other antibiotics, the prescribing information for those agents should be reviewed for contraindications, warnings, precautions and adverse reactions. Renal function should be carefully monitored.

CONTRAINDICATIONS

'Monocid' is contraindicated in persons who have shown hypersensitivity to cephalosporin antibiotics.

WARNINGS

WARNINGS
BEFORE THERAPY WITH 'MONOCID' IS INSTITUTED, CAREFUL INQUIRY
SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD
PREVIOUS HYPERSENSITIVITY REACTIONS TO CEPHALOSPORINS,
PENICILLINS, OR OTHER DRUGS. THIS PRODUCT SHOULD BE GIVEN
CAUTIOUSLY TO PENICILLIN-SENSITIVE PATIENTS. ANTIBIOTICS
SHOULD BE ADMINISTERED WITH CAUTION TO ANY PATIENT WHO HAS
DEMONSTRATED SOME FORM OF ALLERGY, PARTICULARLY TO DRUGS.
SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE
EPINEPHRINE AND OTHER EMERGENCY MEASURES EPINEPHRINE AND OTHER EMERGENCY MEASURES.

Pseudomembranous colitis has been reported with the use of cephalosporins (and other broad-spectrum antibiotics); therefore, it is important to consider that diagnosis in patients who develop diarrhea in association with antibiotic use.

Treatment with broad-spectrum antibiotics alters normal flora of the colon and may permit overgrowth of Clostridia. Studies indicate a toxin produced by *Clostridium difficile* is one primary cause of antibiotic associated colitis. Cholestyramine and colestipol resins have been shown to bind the toxin in vitro.

Mild cases of colitis may respond to drug discontinuance alone. Moderate to severe cases should be managed with fluid, electrolyte and protein supplementation as indicated. When the colitis is not relieved by drug discontinuance and when it is severe, oral vancomycin is the treatment of choice for antibiotic-associated pseudomembranous colitis produced by C. difficile. Other causes of colitis should also be considered.

PRECAUTIONS

General: With any antibiotic, prolonged use may result in overgrowth of nonsusceptible organisms. Careful observation is essential, and appropriate measures should be taken if superinfection occurs.

Drug Interactions: Nephrotoxicity has been reported following concomitant administration of other cephalosporins and aminoglycosides.

Pregnancy: (Category B.) Reproduction studies have been performed in mice, rabbits and rats at doses up to an equivalent of 40 times the usual adult human dose and have revealed no evidence of impaired fertility or harm to the fetus due to 'Monocid'. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used in pregnancy only if clearly needed.

Labor and Delivery: In cesarean section, 'Monocid' should be administered only after the umbilical cord has been clamped.

Nursing Mothers: 'Monocid' is excreted in human milk in low concentrations. Caution should be exercised when 'Monocid' is administered to a nursing woman. Pediatric Use: Safety and effectiveness in children have not been established Beta-lactam antibiotics with methyl-thio-tetrazole side chains have been shown to cause testicular atrophy in prepubertal rats, which persisted into adulthood and resulted in decreased spermatogenesis and decreased fertility. Cefonicid, which contains a methylsulfonic thio tetrazole moiety, has no adverse effect on the male reproductive system of prepubertal, juvenile or adult rats when given under identical conditions.

ADVERSE REACTIONS

'Monocid' is generally well tolerated and adverse reactions have occurred infrequently. The most common adverse reaction has been pain on I.M. injection. On-therapy conditions occurring in greater than 1% of 'Monocid' treated patients were:

 ${\it Injection Site Phenomena~(5.7\%): Pain~and/or~discomfort~on~injection; less~often, burning, phlebitis at I.V.~site.}$

Increased Platelets (1.7%).

Increased Eosinophils (2.9%).

Liver Function Test Alterations (1.6%): Increased alkaline phosphatase, increased SGOT, increased SGPT, increased GGTP, increased LDH.

Less frequent on-therapy conditions occurring in less than 1% of 'Monocid'-treated patients were:

 ${\it Hypersensitivity Reactions:} \ Fever, \ rash, \ pruritus, \ erythema, \ myalgia \ and \ anaphylactoid-type \ reactions \ have been \ reported.$

Hematology: Decreased WBC, neutropenia, thrombocytopenia, positive Coombs' test.

Diarrhea.

DOSAGE AND ADMINISTRATION

General

The usual adult dosage is 1 gram of 'Monocid' given once every 24 hours, intravenously or by deep intramuscular injection. Doses in excess of 1 gram daily are rarely necessary; however, in exceptional cases dosage of up to 2 grams given once daily have been well tolerated. When administering 2 gram I.M. doses once daily, one-half the dose should be administered in different large muscle masses.

Surgical Prophylaxis

When administered one hour prior to appropriate surgical procedures (see Indications and Usage), a 1 gram dose of 'Monocid' provides protection from most infections due to susceptible organisms throughout the course of the procedure and for approximately 24 hours after administration. Intraoperative and postoperative administration of 'Monocid' is not necessary. Daily doses of 'Monocid' may be administered for two additional days in patients undergoing prosthetic arthroplasty or open heart surgery.

In cesarean section 'Monocid' should be administered only after the umbilical cord has been clamped.

General Guidelines for Dosage of 'Monocid', I.V. or I.M.

Type of Infection	Daily Dose (grams)	Frequency
Uncomplicated Urinary Tract	0.5	once every 24 hours
Mild to Moderate	1	once every 24 hours
Severe or Life-Threatening	2*	once every 24 hours
Surgical Prophylaxis	1	1 hour preoperatively

^{*}When administering 2 gram I.M. doses once daily, one half the dose should be administered in different large muscle masses

Impaired Renal Function

Modification of Monocid' dosage is necessary in patients with impaired renal function. Before prescribing, consult Dosage and Administration section of complete prescribing information.

HOW SUPPLIED

"Monocid' is supplied in vials equivalent to 500 mg. and 1 gram of cefonicid; in "Piggyback" Vials for I.V. admixture equivalent to 1 gram of cefonicid; and in Pharmacy Bulk Vials equivalent to 10 grams of cefonicid.

BRS-MC:L15 Date of issuance Fel Date of issuance Feb. 1986

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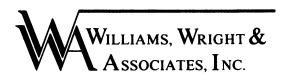
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☐ Pressure normalized[‡] at six months in 86% of patients with mild-to-moderate hypertension (N = 53).§1

☐ Additive antihypertensive effect achieved through complementary actions of ACE inhibition plus thiazide diuresis.

☐ Convenient, one-tablet bid dosage regimen enhances compliance.

†This fixed combination drug is not indicated for initial therapy of hypertension. It may be appropriate if the fixed combination represents the dosage as titrated to the individual patient's needs. In using CAPOZIDE, consideration should be given to the risk of neutropenia agranulocytosis. Use special precautions in patients with impaired renal function, collagen vascular disorders, or those exposed to other drugs known to affect the white cells or immune response. Evaluation of hypertensives should always include assessment of renal function. See INDICATIONS AND USAGE, CONTRAINDICATIONS, WARNINGS, and ADVERSE REACTIONS in the brief summary, which follows.

^{*}Angiotensin Converting Enzyme

[‡]Normalized – diastolic pressure · ≦ 91 mm Hg. [§]Dosage was CAPOZIDE 25-25 (captopril 25 mg and hydrochlorothiazide 25 mg per tablet) bid.

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*Angiotensin Converting Enzyme

References

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CAPOZIDE®

Captopril-Hydrochlorothiazide Tablets

INDICATIONS AND USAGE:—CAPOZIDE (Captopril-Hydrochlorothiazide Tablets) is indicated for the treatment of hypertension. This fixed combination drug is not indicated for initial therapy of hypertension. If the fixed combination represents the dose titrated to the individual patient's needs, it may be more convenient than the separate components. In using CAPOZIDE, consideration should be given to the risk of neutropenia/agranulocylosis (see WARNINGS). CAPOZIDE may be used for patients with normal renal function, in whom the risk is relatively low. In patients with impaired renal function, particularly those with collagen vascular disease, CAPOZIDE should be reserved for hypertensives who have either developed unacceptable side effects on other drugs, or have failed to respond satisfactorily to other drug combinations.

CONTRAINDICATION: Hydrochlorothiazide—Hydrochlorothiazide is contraindicated in patients with anuria and those who have previously demonstrated hypersensitivity to hydrochlorothiazide or other sulfonamide-derived druce.

WIRRNINGS: Captopril—Neutropenia/Agranulocytosis—Neutropenia (<1000/mm³) with myeloid hypoplasia has resulted from use of captopril. About half of the neutropenic patients developed systemic or oral cavity infections or other features of the syndrome of agranulocytosis. The risk of neutropenia is dependent on the clinical status of the patient:

In clinical trials in patients with hypertension who have normal renal function (serum creatinine <1.6 mg/dL and no collagen vascular disease), neutropenia has been seen in one patient out of over 8,600 exposed. In patients with some degree of renal failure (serum creatinine at least 1.6 mg/dL) tho collagen vascular diseases, the risk in clinical trials was about 1 per 500. Doses were relatively high in these patients, particularly in view of their diminished renal function. In patients with collagen vascular diseases (e.g., systemic lupus enythematosus, scleroderma) and impaired renal function, neutropenia occurred in 3.7% of patients in clinical trials. While none of the over 750 patients in formal clinical trials of heart failure developed neutropenia, it has occurred during subsequent clinical experience. Of reported cases, about half had serum creatinine ±1.6 mg/dL and more than 75% received procainamide. In heart failure, it appears that the same risk factors for neutropenia are present. Neutropenia has appeared within 3 months after starting therapy, associated with myeloid hypoplasia and decreated numbers of megakaryocytes (e.g., hypoplastic bone marrow and pancytopenia); anemia and thrombocytopenia were sometimes seen. Neutrophilis generally returned to normal in about 2 weeks after captopril was discontinued, and serious infections were limited to clinically complex patients. About 13% of the cases of neutropenia have ended fatally, but almost all fatalities were in patients with serious illness, having collagen vascular disease, renal failure, heart failure or immunosuppressant therapy, or a combination of these complicating factors.

Evaluation of the hypertensive or heart failure petient should always include assessment of renal function. If captopril is used in patients with impaired renal function, white blood cell and differential counts should be evaluated prior to starting treatment and at approximately 2-week intervals for about 3 months, then periodically. In patients with collagen vascular disease or who are exposed to other drugs known to affect the white cells or immune response, particularly when there is impaired renal function, captopril should be used only after an assessment of benefit and risk, and then with caution. All patients treated with captopril should be told to report any signs of infection (e.g., sore throat, lever); if infection is suspected, perform counts without delay. Since discontinuation of captopril and other drugs has generally led to prompt return of the white count to normal, upon confirmation of neutropenia (neutrophil count <1000/mm²) withdraw captopril and closely follow the patient's course.

Proteinuria—Total urinary proteins > 1 g/day were seen in about 0.7% of patients on captopril. About

Proteinuria—Total urinary proteins >1 g/day were seen in about 0.7% of patients on captopril. About 90% of affected patients had evidence of prior renal disease or received high doses (>150 mg/day), or both. The nephrotic syndrome occurred in about one-fifth of proteinuric patients. In most cases, proteinuria subsided or cleared within 6 months whether or not captopril was continued. The BUN and creatine were seldom altered in proteinuric patients. Since most cases of proteinuria occurred by the 8th month of therapy, patients with prior renal disease or those receiving captopril at doses >150 mg/day should have urinary protein estimates (dip-stick on 1st morning urine) before therapy, and periodically thereafter. Hypotension—Excessive hypotension was rarely seen in hypertensive patients but is a possibility in severely salf/votume-depleted persons such as those treated vigorously with diuretics (see PRECAU-TONS fibrun Interactions).

Hydrochlorothlazide—Use with caution in severe renal disease. May precipitate azotemia in patients with renal disease. Cumulative effects may develop in patients with impaired renal function. Use with caution in patients with impaired hepatic function or progressive liver disease, since minor afterations of fluid and electrolyte balance may precipitate hepatic coma. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

PRECAUTIONS: General: Captopril—Impaired Renal Function—Some patients with renal disease, particularly those with severe renal artery stenosis, have developed increases in BUN and serum creatinine. It may be necessary to reduce captopril dosage and/or discontinue diuretic. For some of these patients, normalization of blood pressure and maintenance of adequate renal perfusion may not be possible (see DOSAGE AND ADMINISTRATION, ADVERISE REACTIONS [Altered Laboratory Findings]). Surgery/Anesthesia—If hypotension occurs during major surgery or anesthesia, and is considered due to the effects of captopril, it is correctable by volume expansion.

to the effects of captopril, it is correctable by volume expansion.

Hydrochlorothiacide—Observe all patients for signs of fluid or electrolyte imbalance, particularly when the patient is voniting excessively or receiving parenteral fluids. Warning signs include dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and nausea and vomiting. Hypokalemia may develop when severe cirrhosis is present or without adequate oral electrolyte intake. Hypokalemia can sensitize or exaggerate response of the heart to the toxic effects of digitalis. Because captopril reduces the production of adosterone, concomitant therapy with captopril reduces the diuretic-induced hypokalemia. Fewer patients may require potassium supplements and/or foods with a high potassium content (see Drug Interactions, Agents Increasing Serum Potassium).

Any chloride deflicit is generally mild and may not require specific treatment, exceptions include liver

Any chloride delicit is generally milic and may not require specific treatment, exceptions include liver disease or renal disease. Dilutional hyponatremia may occur in edematious patients in hot weather; use water restriction, rather than salt administration except when the hyponatremia is life-threatening. In actual salt depletion, replacement is the therapy of choice. Hyperuricemia may occur or frank gout may be precipitated in certain patients. Latent diabetes mellitus may become manifest. Antihypertensive effects may be enhanced in the postsympathectomy patient. Progressive renal impairment, indicated by rising nonprotein nitrogen or blood urea nitrogen, requires a careful reappraisal of the necessity of therapy. Serum PBI levels may decrease. Calcium excretion is decreased. Pathologic changes in the parathyroid gland with hypercalcemia and hypophosphatemia have been observed during prolonged therapy. Laboratory Tests—Serum and urine electrolyte levels should be regularly monitored (see WARNINGS, (Captopril and Hydrochlorothiazide), also PRECAUTIONS (Generat, Hydrochlorothiazide).

Drug Interactions—Captopril—Hypotension—Patients on Diuretic Therapy: Precipitous reduction of blood pressure may occasionally occur within the 1st hour after administration of the initial captopril dose in patients on diuretics, especially those recently placed on diuretics, and hose on severe dietary salt restriction or dialysis. This possibility can be minimized by either discontinuing the diuretic or increasing the salt intake about 1 week prior to initiation of captopril therapy or by initiating therapy with small doses (6.25 or 12.5 mg). Alternatively, provide medical supervision for at least 1 hour after the initial dose. Agents Having Vasodilator Activity: In heart failure patients, vasodilators should be administered with caution. Agents Causing Renin Release: Captoprils effect will be augmented by antihypertensive agents that cause renin release. Agents Affecting Sympathetic Activity: The sympathetic nervous system may be especially important in supporting blood pressure in patients receiving captopril atone or with diuretics. Beta-adrenegic blocking drugs add some further arithypertensive effect to captopril, but the overall response is less than additive. Therefore, use agents affecting sympathetic activity (e.g., ganglionic blocking agents or adrenergic neuron blocking agents), with caution. Agents converned

hypokalemia, and then with caution, since they may lead to a significant increase of serum potassium. Use potassium-containing sall substitutes with caution. *Inhibitors Of Endogenous Prostaglandin Synthesis*: Indomethacin and other nonsteroidal anti-inflammatory agents may reduce the antihypertensive effect of captopril, especially in low renin hypertension.

Hydrochlorothiazide—When administered concurrently the following drugs may interact with thiazide diuretics: Alcohol, barbiturates, or narcotics—potentiation of orthostatic hypotension may occur. Antidiabetic drugs (oral agents and insulin)—Hyperglycemia induced by thiazides may require dosage adjustment of the antidiabetic drug. Other antihypertensive drugs—additive effect or potentiation. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs. Corticosteroids, ACTH—intensified electrohyte depletion, particularly hypokalemia. Preasesthetic and anesthetic agents may be potentiated; adjust dosage of these agents accordingly. Pressor amines (e.g., norepinephrine)—possible decreased response to pressor amines but not sufficient to predude their use. Skeletal muscle relaxants, nondepolarizing (e.g., tubocurarine)—possible increased responsiveness to the muscle relaxant. Lithium—should not generally be given with diuretics; diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity. Refer to the package insert for lithium preparations before use of such preparations with CAPOZIDE.

Drug/Laboratory Test Interactions—Captopril—may cause a false-positive urine test for acetone.

Drug/Laboratory Test Interactions—Captopril—may cause a false-positive urine test for acetone. Hydrochlorothiazide—Discontinue thiazides before carrying out tests for parathyroid function (see PRECAUTIONS [General, Hydrochlorothiazide]).

Carcinogenesis, Mutagenesis and Impairment of Fertility—Captopril—Two-year studies with doses of 50 to 1350 mg/kg/day in mice and rats failed to show any evidence of carcinogenic potential. Studies in rats have revealed no impairment of fertility.

Hydrochlorothiazide—Long-term studies in animals have not been performed to evaluate carcinogenic potential, mutagenesis, or whether this drug affects fertility in males or females.

Pregnancy: Category C—Captopril—There are no adequate and well-controlled studies in pregnant women. Embryocidal effects and craniclacial malformations were observed in rabbits. Therefore, captopril should be used during pregnancy only if the potential benefit outweighs the potential risk to the fetus. Captopril crosses the human placenta.

Hydrochlorothiazide—Studies in pregnant rats using captopril and hydrochlorothiazide individually and in combination, each agent in doses up to 1350 mg/kg, failed to show evidence of embryotoxicity, tetotoxicity, or teratogenicity. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, CAPO2IDE should be used during pregnancy, or in patients likely to become pregnant, only if the potential benefit justifies the potential risk to the fetus.

Pregnancy—Nonteratogenic Effects—Hydrochlorothiazide—Thiazides cross the placental barrier

Pregnancy—Nonteratogenic Effects—Hydrochlorothlazide—Thiazides cross the placental barrier and appear in cord blood. Use in pregnant women requires that the benefit be weighed against possible hazards to the fetus. Hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other reported reactions.

Nursing Mothers: Both captopril and hydrochlorothiazide are excreted in human milk. A potential exists for serious adverse reactions in nursing infants from both drugs, therefore, decision whether to discontinue nursing or to discontinue therapy should take into account the importance of CAPOZIDE (Captopril-Hydrochlorothiazide Tablets) to the mother.

Pediatric Use: Safety and effectiveness in children have not been established although there is limited experience with use of captopril in children from 2 months to 15 years of age. Dosage, on a weight basis, was comparable to that used in adults. CAPOZIDE should be used in children only if other measures for controlling blood pressure have not been effective.

ADVERSE REACTIONS: Captopril—Reported incidences are based on clinical trials involving approximately 7000 patients. *Benal*—About 1 of 100 patients developed proteinuria (see WARNINGS). Renal insufficiency, renal failure, polyuria, oliguria, and urinary frequency in 1 to 2 of 1000 patients. *Hernatologic*—Neutropenia/agranulocytosis has occurred (see WARNINGS). Anemia, thrombocytopenia, and pancytopenia have been reported. *Dermatologic*—Rash (usually maculopapular, rarely urticarial), often with pruritus and sometimes with lever and eosinophilia, in about 4 to 7 of 100 patients (depending on renal status and dose), usually during the 1st 4 weeks of therapy. Pruritus, without rash, in about 2 of 100 patients. A reversible associated pemphigoid-like lesion, and photosensitivity have also been reported. Angioedema of the face, mucous membranes of the mouth, or of the extremities in about 1 of 1000 patients—reversible on discontinuance of captopril therapy. One case of laryngeal edema reported. Flushing or pallor in 2 to 5 of 1000 patients. *Cardiovascular*—Hypotension may occur, see WARNINGS and PRECAUTIONS (Drug Interactions) for discussion of hypotension on initiation captopril therapy. Tachycardia, chest pain, and palpitations each in about 1 of 100 patients. Angina pectoris, myocardial infarction, Raynaud's syndrome, and congestive heart failure each in 2 to 3 of 1000 patients. *Dysgusia*—About 2 to 4 (depending on renal status and dose) of 100 patients developed a diminution or loss of taste perception; taste impairment is reversible and usually self-limited even with continued drug use (2 to 3 months). Gastric irritation, abdominal pain, nausea, vorniting, diarrhea, anorexia, constipation, apthhous ulcers, peptic ulcer, dizziness, headache, malaise, fatigue, insomnia, dry mouth, dyspnea, cough, alopecia, and paresthesias reported in about 0.5 to 2% of patients but did not appear at increased frequency compared to placebo or other freatments used in controlled trials.

Hydrochlorothlazide – Gastrointestinal System – anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (infrahepatic cholestatic jaundice), pancreatitis, and sialadentis. Central Nervous System – dizziness, vertigo, paresthesias, headache, and xanthopsia. Hematologic – leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia, and hemolytic anemia. Cardiovascular—orthostatic hypotension. Hypersensitivity – purpura, photosensitivity, rash, urticaria, necrotizing angilisi (vasculitis; cutaneous vasculitis), lever, respiratory distress including pneumonitis, and anaphylactic reactions. Other—hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness, and transient blurred vision. Whenever adverse reactions are moderate or severe, reduce or withdraw theraov.

Altered Laboratory Findings: Elevations of liver enzymes have been noted in a few patients but no causal relationship to captopril use has been established. Rare cases of cholestatic jaundice and of hepatocellular injury with or without secondary cholestasis have been reported in association with captopril administration. A transient elevation of BUN and serum creatinine may occur, especially in patients who are volume-depleted or who have renovascular hypertension. In instances of rapid reduction of longstanding or severely elevated blood pressure, the glomerular filtration rate may decrease transiently, also resulting in transient rises in serum creatinine and BUN. Small increases in the serum potassium concentration frequently occur, especially in patients with renal impairment (see PRECAUTIONS).

OVERDOSAGE: Captopril—Primary concern is correction of hypotension. Volume expansion with an LV influsion of normal saline is the treatment of choice for restoration of blood pressure. Captopril may be removed from the openeral circulation by hemodialysts.

Hydrochlorothiazide—In addition to diuresis, overdosage of thiazides may produce varying degrees of lethargy which may progress to come within a few hours, with minimal respiratory and cardiovascular depression and without evidence of serum electrolyte changes or dehydration. The mechanism of thiazide-induced CNS depression is unknown. Gastrointestinal irritation and hypermotility may occur, ransitory increase in BUN has been reported, and serum electrolyte changes may occur, especially in patients with impaired renal function. In addition to gastric lavage and supportive therapy for stupor or coma, symptomatic treatment of gastrointestinal effects may be needed. Degree of removal by hemodialysis has not been clearly established. Measures to maintain hydration, electrolyte balance, respiration, and cardiovascular and renal function should be instituted.

DOSAGE AND ADMINISTRATION: DOSAGE MUST BE INDIVIDUALIZED (SEE INDICATIONS AND US-AGE). CAPOZIDE (Captopril-Hydrochiorothiazide Tablets) should be taken one hour before meats. CAPOZIDE may be dosed bid or tid. Because captopril and hydrochiorothiazide are excreted primarily by the kidneys, dosage adjustments are recommended for patients with impaired renal function. Consult package insert before prescribing CAPOZIDE (Captopril-Hydrochlorothiazide Tablets).

Consult package insert before prescribing CAPUZIDE (Captopril-Hydrochlorothjazide Tablets). Available in tablets of 25 mg captopril combined with 15 mg hydrochlorothjazide, 25 mg captopril combined with 25 mg hydrochlorothjazide, 50 mg captopril combined with 15 mg hydrochlorothjazide, and 50 mg captopril combined with 25 mg hydrochlorothjazide in bottles of 100. (14-005C)



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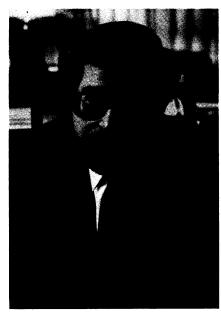
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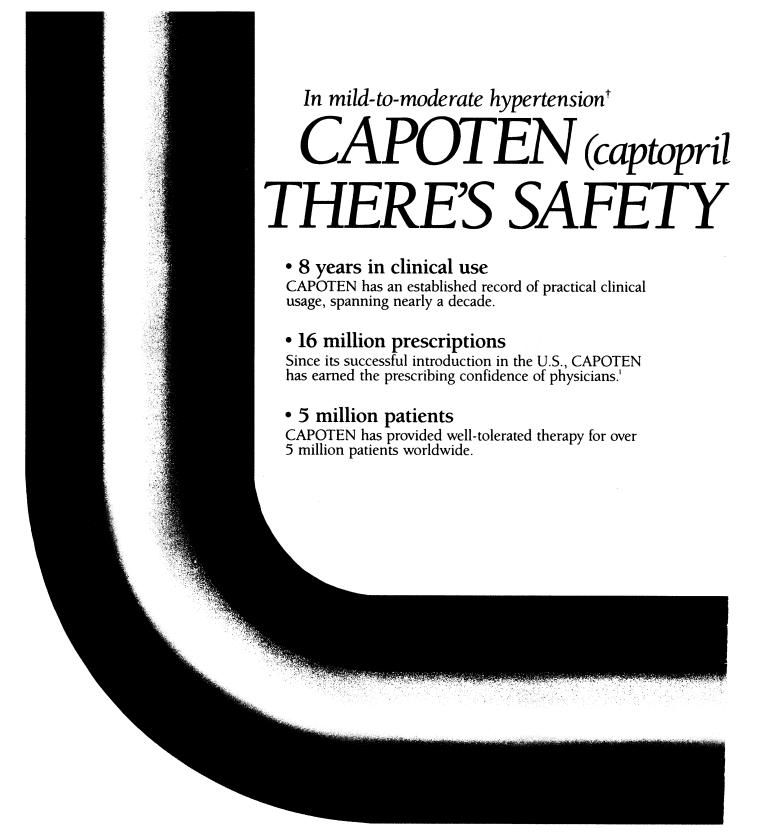


"Already, we've been talking to a lot of physicians and hospitals face-to-face, getting their input on how we can become a more service-oriented organization. Their biggest concern is that our claim payments are on the slow side. And they're right. But I can honestly say improvements with that are already in the works. As far as individual and group plans go, they seem to like what we're doing. They understand that as hard as it is today to keep costs down, no one is doing a better job."



"We're in this together. We can't function without the hospitals and physicians, and vice-versa, they can't operate without us. And it's true, times are tough right now. But recently I was elected to the Board of Directors of the Southern California Hospital Association. So there's an exchange going on of thoughts and ideas. And that's encouraging. It can only make things better. After all, our goal is to make it as easy as possible for hospitals. To always be there when they need us. And I think we're heading in the right direction."





†CAPOTEN may be used as initial therapy only for patients with normal renal function in whom the risk of neutropenia/agranulocytosis is relatively low (1 out of over 8,600 in clinical trials). Use special precautions in patients with impaired renal function, collagen vascular disorders, or those exposed to other drugs known to affect the white cells or immune response. Evaluation of hypertensives should always include assessment of renal function. See INDICATIONS AND USAGE, WARNINGS, and ADVERSE REACTIONS in the brief summary on the adjacent page.



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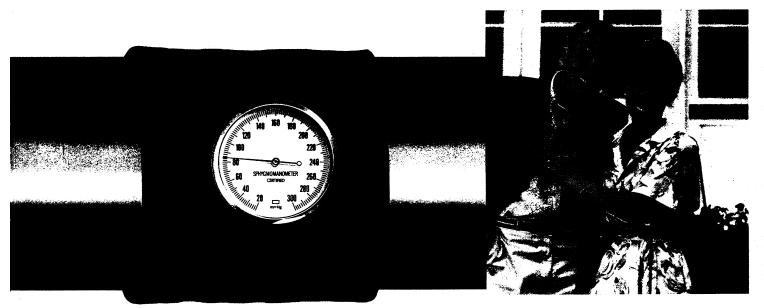
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Comparison of Adverse Effects for CAPOTEN (\le 100 mg) versus Placebo in Hypertensive Patients with Normal Renal Function (N=1,622) ‡ ?

ADVERSE EFFECT	CAPOTEN (N = 1,174) (% affected)	Placebo (N = 448) (% affected)
Headache	5.2	6.9
Rash	3.7	2.5
Dizziness	3.5	2.0
Nausea	3.2	2.0
Fatigue	3.1	2.0
Taste alteration	1.5	1.1
Gastrointestinal	1.4	0.7
Diarrhea	1.1	1.1

*None of the differences between captopril and placebo was statistically significant. For the most part, adverse effects were mild and transient and usually did not require discontinuation of therapy. Only 5.5% of the patients in this data base discontinued because of an adverse effect. Data include adverse effects for CAPOTEN with an incidence greater than 1%.



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captopril tablets

FIRST-LINE THERAPY THAT PUTS QUALITY OF LIFE FIRST

INDICATIONS: Hypertension — CAPOTEN (captopril) is indicated for the treatment of hypertension. Consideration should be given to the risk of neutropenia/agranulocytosis (see WARNINGS). CAPOTEN may be used as initial therapy for patients with normal renal function, in whom the risk is relatively low. In patients with impaired renal function, particularly those with collagen vascular disease, captopril should be reserved for those who have either developed unacceptable side effects on other drugs, or have failed to respond satisfactorily to drug combinations. CAPOTEN is effective alone and in combination with other antihypertensive agents, especially thiazide-type diuretics.

Heart Failure: CAPOTEN (captopril) is indicated in patients with heart failure who have not responded adequately to or cannot be controlled by conventional diuretic and digitalis therapy. CAPOTEN is to be used with diuretics and digitalis.

WARNINGS: Neutropenia/Agranulocytosis — Neutropenia (<1000/mm³) with myeloid hypoplasia has resulted from use of captopril. About half of the neutropenic patients developed systemic or oral cavity infections or other features of the syndrome of agranulocytosis. The risk of neutropenia is dependent on the clinical status of the patient:

In clinical trials in patients with hypertension who have normal renal function (serum creatinine < 1.6 mg/dL and no collagen vascular disease), neutropenia has been seen in one patient out of over 8,600 exposed. In patients with some degree of renal failure (serum creatinine at least 1.6 mg/dL) but no collagen vascular disease, the risk in clinical trials was about 1 per 500. Doses were relatively high in these patients, particularly in view of their diminished renal function. In patients with collagen vascular diseases (e.g., systemic lupus crythematosus, scleroderma) and impaired renal function, neutropenia occurred in 3.7% of patients in clinical trials. While none of the over 750 patients in formal clinical trials of heart failure developed neutropenia, it has occurred during subsequent clinical experience. Of reported cases, about half had serum creatinine ≥ 1.6 mg/dL and more than 75% received procainamide. In heart failure, it appears that the same risk factors for neutropenia are present.

Neutropenia has appeared usually within 3 months after starting therapy, associated with myeloid hypoplasia and frequently accompanied by erythroid hypoplasia and decreased numbers of megakaryocytes (e.g., hypoplastic bone marrow and pancytopenia); anemia and thrombocytopenia were sometimes seen. Neutrophils generally returned to normal in about 2 weeks after captopril was discontinued, and serious infections were limited to clinically complex patients. About 13% of the cases of neutropenia have ended fatally, but almost all fatalities were in patients with serious illness, having collagen vascular disease, renal failure, heart failure or immunosuppressant therapy, or a combination of these complicating factors.

Evaluation of the hypertensive or heart failure patient should always include assessment of renal function. If captopril is used in patients with impaired renal function, white blood cell and differential counts should be evaluated prior to starting treatment and at approximately 2-week intervals for about 3 months, then periodically. In patients with collagen vascular disease or who are exposed to other drugs known to affect the white cells or immune response, particularly when there is impaired renal function, captopril should be used only after an assessment of benefit and risk, and then with caution. All patients treated with captopril should be told to report any signs of infection (e.g., sore throat, fever); if infection is suspected, perform counts without delay. Since discontinuation of captopril and other drugs has generally led to prompt return of the white count to normal, upon confirmation of neutropenia (neutrophil count < 1000/mm³) withdraw captopril and closely follow the natient's course.

Proteinuria — Total urinary proteins >1 g/day were seen in about 0.7% of patients on captopril. About 90% of affected patients had evidence of prior renal disease or received high doses (>150 mg/day), or both. The nephrotic syndrome occurred in about one-fifth of proteinuric patients. In most cases, proteinuria subsided or cleared within 6 months whether or not captopril was continued. The BUN and creatinine were seldom altered in proteinuric patients. Since most cases of proteinuria occurred by the 8th month of therapy, patients with prior renal disease or those receiving captopril at doses >150 mg/day should have urinary protein estimates (dip-stick on lst morning urine) before therapy, and periodically thereafter.

Hypotension – Excessive hypotension was rarely seen in hypertensive patients but is a possibility in severely salt/volume-depleted persons such as those treated vigorously with diuretics (see PRECAUTIONS [Drug Interactions]).

In heart failure, where blood pressure was either normal or low, transient decreases

In heart failure, where blood pressure was either normal or low, transient decreases in mean blood pressure >20% were recorded in about half of the patients. This transient hypotension may occur after any of the first several-doses and is usually well tolerated, although rarely it has been associated with arrhythmia or conduction defects. A starting dose of 6.25 or 12.5 mg tid may minimize the hypotensive effect. Patients should be followed closely for the first 2 weeks of treatment and whenever the dose of captopril and/or diuretic is increased.

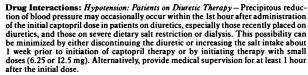
BECAUSE OF THE POTENTIAL FALL IN BLOOD PRESSURE IN THESE PATIENTS, THERAPY SHOULD BE STARTED UNDER VERY CLOSE MEDICAL SUPERVISION.

PRECAUTIONS: General: Impaired Renal Function, Hypertension—Some hypertensive patients with renal disease, particularly those with severe renal artery stenosis, have developed increases in BUN and serum creatinine. It may be necessary to reduce captopril dosage and/or discontinue diuretic. For some of these patients, normalization of blood pressure and maintenance of adequate renal perfusion may not be possible. Heart Failure—About 20% of patients develop stable elevations of BUN and serum creatinine >20% above normal or baseline upon long-term treatment. Less than 5% of patients, generally with severe preexisting renal disease, required discontinuation due to progressively increasing creatinine. See DOSAGE AND ADMINISTRATION, ADVERSE REACTIONS [Altered Laboratory Findings]. Valuular Stenosis—A theoretical concern, for risk of decreased coronary perfusion, has been noted regarding vasodilator treatment in patients with aortic stenosis due to decreased afterload reduction.

 ${\it Surgery/Anesthesia} - If \ hypotension occurs during \ major \ surgery \ or \ anesthesia, and \ is \ considered \ due \ to \ the \ effects \ of \ captopril, \ it \ is \ correctable \ by \ volume \ expansion.$

References:

- 1. PDS Alpha, National Prescription Report, Pharmaceutical Data Services, Subsidiary of McKesson Corporation.
- 2. Data on file, Squibb Institute for Medical Research.



 $\label{eq:Agents} \textit{Agents Having Vasodilator Activity} - \text{In heart failure patients, vasodilators should} \\ \text{be administered with caution.}$

Agents Causing Renin Release — Captopril's effect will be augmented by antihypertensive agents that cause renin release.

Agents Affecting Sympathetic Activity—The sympathetic nervous system may be especially important in supporting blood pressure in patients receiving captopril alone or with diuretics. Beta-adrenergic blocking drugs add some further antihypertensive effect to captopril, but the overall response is less than additive. Therefore, use agents affecting sympathetic activity (e.g., ganglionic blocking agents or adrenergic neuron blocking agents) with caution.

Agents Increasing Serum Potassium — Give potassium-sparing diuretics or potassium supplements only for documented hypokalemia, and then with caution, since they may lead to a significant increase of serum potassium. Use potassium-containing salt substitutes with caution.

Inhibitors of Endogenous Prostaglandin Synthesis – Indomethacin and other nonsteroidal anti-inflammatory agents may reduce the antihypertensive effect of captopril, especially in low renin hypertension.

Drug/Laboratory Test Interaction: Captopril may cause a false-positive urine test for acetone.

Carcinogenesis, Mutagenesis and Impairment of Fertility: Two-year studies with doses of 50 to 1350 mg/kg/day in mice and rats failed to show any evidence of carcinogenic potential. Studies in rats have revealed no impairment of fertility.

Pregnancy: Category C – There are no adequate and well-controlled studies in pregnant women. Embryocidal effects and craniofacial malformations were observed in rabbits. Therefore, captopril should be used during pregnancy, or for patients likely to become pregnant, only if the potential benefit outweighs the potential risk to the fetus. Captopril crosses the human placenta.

Nursing Mothers: Captopril is secreted in human milk. Exercise caution when administering captopril to a nursing woman, and, in general, nursing should be interrupted.

Pediatric Use: Safety and effectiveness in children have not been established although there is limited experience with use of captopril in children from 2 months to 15 years of age. Dosage, on a weight basis, was comparable to that used in adults. Captopril should be used in children only if other measures for controlling blood pressure have not been effective.

ADVERSE REACTIONS: Reported incidences are based on clinical trials involving approximately 7000 patients.

Renal — About 1 of 100 patients developed proteinuria (see WARNINGS). Renal insufficiency, renal failure, polyuria, oliguria, and urinary frequency in 1 to 2 of 1000 patients.

Hematologic – Neutropenia/agranulocytosis have occurred (see WARNINGS). Anemia, thrombocytopenia, and pancytopenia have been reported.

Dermatologic — Rash (usually maculopapular, rarely urticarial), often with pruritus and sometimes with fever and cosinophilia, in about 4 to 7 of 100 patients (depending on renal status and dose), usually during the 1st 4 weeks of therapy. Pruritus, without rash, in about 2 of 100 patients. A reversible associated pemphigoid-like lesion, and photosensitivity have also been reported. Angioedema of the face, mucous membranes of the mouth, or of the extremities in about 1 of 1000 patients — reversible on discontinuance of captopril therapy. One case of laryngeal edema reported. Flushing or pallor in 2 to 5 of 1000 patients.

Cardiovascular — Hypotension may occur, see WARNINGS and PRECAUTIONS (Drug Interactions) for discussion of hypotension on initiation of captopril therapy. Tachycardia, chest pain, and palpitations each in about 1 of 100 patients. Angina pectoris, myocardial infarction, Raynaud's syndrome, and congestive heart failure each in 2 to 3 of 1000 patients.

Dysgeusia – About 2 to 4 (depending on renal status and dose) of 100 patients developed a diminution or loss of taste perception; taste impairment is reversible and usually self-limited even with continued drug use (2 to 3 months). Gastric irritation, abdominal pain, nausea, vomiting, diarrhea, annorexia, constipation, aphthous ulcers, peptic ulcer, dizziness, headache, malaise, fatigue, insomnia, dry mouth, dyspnea, cough, alopecia, and paresthesias reported in about 0.5 to 2% of patients but did not appear at increased frequency compared to placebo or other treatments used in controlled trials.

Altered Laboratory Findings: Elevations of liver enzymes in a few patients although no causal relationship has been established. Rarely cholestatic jaundice and hepatocellular injury with or without secondary cholestasis, have been reported. A transient elevation of BUN and serum creatinine may occur, especially in volume-depleted or renovascular hypertensive patients. In instances of rapid reduction of longstanding or severely elevated blood pressure, the glomerular filtration rate may decrease transiently, also resulting in transient rises in serum creatinine and BUN. Small increases in serum potassium concentration frequently occur, especially in patients with renal impairment (see PRECAUTIONS).

OVERDOSAGE: Primary concern is correction of hypotension. Volume expansion with an I.V. infusion of normal saline is the treatment of choice for restoration of blood pressure. Captopril may be removed from the general circulation by hemodialysis.

DOSAGE AND ADMINISTRATION: CAPOTEN (captopril) should be taken one hour before meals. In hypertension, CAPOTEN may be dosed bid or tid. Dosage must be individualized; see DOSAGE AND ADMINISTRATION section of package insert for detailed information regarding dosage in hypertension and in heart failure. Because CAPOTEN (captopril) is excreted primarily by the kidneys, dosage adjustments are recommended for patients with impaired renal function.

Consult package insert before prescribing CAPOTEN (captopril).

HOW SUPPLIED: Available in tablets of 12.5, 25, 50, and 100 mg in bottles of 100 (25 mg also available in bottles of 1000), and in UNIMATIC* single dose packs of 100 tablets. (J3-658D)





We Wrote the Books on Patient Medication Education...





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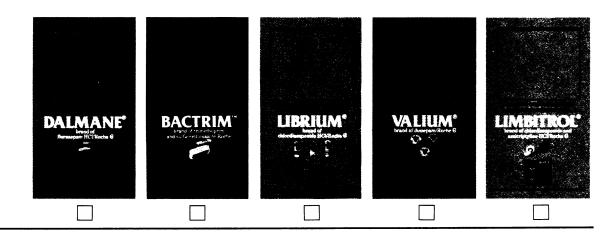
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Before prescribing, see complete prescribing information in SK&F CO. literature or *PDR*. The following is a brief summary.

WARNING

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: Concomitant use with other potassium-sparing agents such as spironolactone or amiloride. Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamidederived drugs.

derived drugs.

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ili, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K* levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict t* intake. Associated widened ORS complex or arrhythmia requires prompt additional therapy. Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus has been reported with thiazide diuretics.

Precautions: The bioavailability of the hydrochlorothiazide component of

out a history of allergy of bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus has been reported with thiazide diuretics.

Precautions: The bioavailability of the hydrochlorothiazide component of 'Dyazide' is about 50% of the bioavailability of the single entity. Theoretically a patient transferred from the single entities of triamterene and hydrochlorothiazide may show an increase in blood pressure or fluid retention. Similarly, it is also possible that the lesser hydrochlorothiazide bioavailability could lead to increased serum potassium levels. However, extensive clinical experience with 'Dyazide' suggests that these conditions have not been commonly observed in clinical practice. Angiotensin converting enzyme (ACE) inhibitors can elevate serum potassium, use with caution with 'Dyazide'. Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids, and during concurrent use with amphotericin B or corticosteroids or corticostropin (ACTHI). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Cumulative effects of the drug may develop in patients with impaired renal function. Thazides should be used with caution in patients with impaired repatic function. They can precipitate coma in patients with impaired renal function. Thiazides should be used with caution in patients with impaired renal function. Thiazides in patients with a patient in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic and hemolytic anemia have been reported in patients receiving triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly Antihypertensive effects may be encessary. Clinically insignificant reductions in arterial responsiveness to norepinephrine have been reported. Thiazides have also been shown to increase the paralyzing effect

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances; postural hypotension (may be aggravated by alcohol, barbiturates, or narcotics). Necrotizing vasculitis, paresthesias, icteus, pancreatilis, anathopsia and respiratory distress including pneumonitis and pulmonary edema, transient blurred vision, sialadenitis, and vertigo have occurred with thiazides alone. Triamterene has been found in renal stones in association with other usual calculus components. Rare incidents of acute interstitial nephritis have been reported. Impotence has been reported in a few patients on "Dyazide", although a causal relationship has not been established.

Supplied: 'Dyazide' is supplied as a red and white capsule, in bottles of 1000 capsules; Single Unit Packages (unit-dose) of 100 (intended for institutional use only); in Patient-Pak™ unit-of-use bottles of 100.

BRS-DZ:L42

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The unique red and white Dyazide* capsule: Your assurance of SK&F quality.



In Hypertensives Over 50, Diuretics Are Preferred

The 1984 Report of the Joint National Committee on Detection. Evaluation, and Treatment of High Blood Pressure recommends diuretics as the favored monotherapy in patients over 50 years of age, regardless of sex or race.



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Serum K⁺ and BUN should be checked periodically (see Warnings and Precautions).

FOR HYPERTENSIVE PATIENTS INTOLERANT OF BETA-BLOCKER THERAPY

CONSIDER

VASOTEC



For a Brief Summary of Prescribing Information, please see last page of this advertisement.

IT MAY CHANGE THE WAY YOUR PATIENTS FEEL ON



VASOTEC* (Enalapril Maleate, MSD) is contraindicated in patients who are hypersensitive to this product.

ANTIHYPERTENSIVE THERAPY

- Certain subjective symptoms such as malaise and drowsiness, which may interfere with physical or mental activity, have not been characteristic of VASOTEC. This may be related to the specificity of action of VASOTEC on the renin-angiotensin-aldosterone system.
- In worldwide controlled clinical trials, VASOTEC was generally well tolerated. The overall percentage of patients reporting adverse effects was comparable to placebo.
- For the most part, adverse effects in clinical trials were mild and transient and usually did not require discontinuation of therapy.

Angioedema has been reported in patients treated with angiotensin-convertingenzyme inhibitors, including VASOTEC (0.2% of patients treated with VASOTEC). Angioedema associated with laryngeal edema and/or shock may be fatal. If laryngeal stridor or angioedema of the face, tongue, or glottis occurs, treatment with VASOTEC should be discontinued and appropriate therapy instituted immediately (see ADVERSE REACTIONS).

Hypersensitivity to catecholamines has been observed in patients withdrawn from beta-blocker therapy; exacerbation of angina and, in some cases, myocardial infarction have occurred after <u>abrupt</u> discontinuation of such therapy. Therefore, discontinue therapy with a beta blocker only in accordance with the recommendations in the prescribing information for that product. Begin therapy with VASOTEC on the day following the last day of therapy with the beta blocker.



FOR MANY HYPERTENSIVE PATIENTS ONCE-A-DAY



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For a Brief Summary of Prescribing Information, please see next page of this advertisement.



FOR MANY HYPERTENSIVE PATIENTS ONCE-A-DAY VASOTEC

(ENALAPRIL MALEATE MSD)

Contraindications: VASOTEC* (Enalapril Maleate, MSD) is contraindicated in patients who are hypersensitive to this product.

Warnings: Angioedema: Angioedema has been reported in patients treated with angiotensin-converting-enzyme inhibitors, including VASOTEC. Angioedema associated with laryngeal edema and/or shock may be fatal. If laryngeal stridor or angioedema of the face, tongue, or glottis occurs, treatment with VASOTEC should be discontinued and appropriate therapy instituted immediately. (See ADVERSE REACTIONS.)

Hypotension: Excessive hypotension was rarely seen in uncomplicated hypertensive patients but is a possible consequence of enalapril use in severely salt/volume-depleted persons such as those treated vigorously with diuretics or patients on dialysis. (See PRE-CAUTIONS, Drug Interactions and ADVERSE REACTIONS.) In patients with severe congestive heart failure, with or without associated renal insufficiency, excessive hypotension has been observed and may be associated with oliguria and/or progressive azotemia, and rarely with acute renal failure and/or death. Because of the potential fall in blood pressure in these patients, therapy should be started under very close medical supervision. Such patients should be followed closely for the first two weeks of treatment and whenever the dose of enalapril and/or diuretic is increased.

If hypotension occurs, the patient should be placed in supine position and, if necessary, receive an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further doses, which usually can be given without difficulty once the blood pressure has increased after volume expansion.

Neutropenia/Agranulocytosis: Another angiotensin-converting-enzyme inhibitor has been shown to cause agranulocytosis and bone marrow depression, rarely in uncomplicated patients but more frequently in patients with renal impairment, especially if they also have a collagen vascular disease. Available data from clinical trials of enalapril are insufficient to show that enalapril does not cause agranulocytosis at similar rates. Foreign marketing experience has revealed several cases of neutropenia or agranulocytosis in which a causal relationship to enalapril cannot be excluded. Periodic monitoring of white blood cell counts in patients with collagen vascular disease and renal disease should be considered.

Precautions: General: Impaired Renal Function: In clinical studies in hypertensive patients with unilateral or bilateral renal artery stenosis, increases in blood urea nitrogen and serum creatinine were observed in 20% of patients. These increases were almost always reversible upon discontinuation of enalapril and/or diuretic therapy. In such patients renal function should be monitored during the first few weeks of therapy.

Some hypertensive patients with no apparent preexisting renal vascular disease have developed increases in blood urea and serum creatinine, usually minor and transient, especially when VASOTEC has been given concomitantly with a diuretic. This is more likely to occur in patients with preexisting renal impairment. Dosage reduction of VASOTEC and/or discontinuation of the diuretic may be required.

Hyperkalemia: Elevated serum potassium (greater than 5.7 mEq/L) was observed in approximately 1% of hypertensive patients in clinical trials. In most cases these were isolated values which resolved despite continued therapy. Hyperkalemia was a cause of discontinuation of therapy in 0.28% of hypertensive patients. Risk factors for the development of hyperkalemia may include renal insufficiency, diabetes mellitus, and the concomitant use of agents to treat hypokalemia. (See *Drug Interactions*.)

Surgery/Anesthesia: In patients undergoing major surgery or during anesthesia with agents that produce hypotension, enalapril may block angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

Information for Patients.

Angioedema: Angioedema, including laryngeal edema, may occur especially following the first dose of enalapril. Patients should be so advised and told to report immediately any signs or symptoms suggesting angioedema (swelling of face, eyes, lips, tongue, difficulty in breathing) and to take no more drug until they have consulted with the prescribing physician.

Hypotension: Patients should be cautioned to report lightheadedness especially during the first few days of therapy. If actual syncope occurs, the patients should be told to discontinue the drug until they have consulted with the prescribing physician.

All patients should be cautioned that excessive perspiration and dehydration may lead to an excessive fall in blood pressure because of reduction in fluid volume. Other causes of volume depletion such as vomiting or diarrhea may also lead to a fall in blood pressure; patients should be advised to consult with the physician.

Neutropenia: Patients should be told to report promptly any indication of infection (e.g., sore throat, fever) which may be a sign of neutropenia.

NOTE: As with many other drugs, certain advice to patients being treated with enalapril is warranted. This information is intended to aid in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects.

Drug Interactions:

Hypotension: Patients on Diuretic Therapy: Patients on diuretics and especially those in whom diuretic therapy was recently instituted may occasionally experience an excessive reduction of blood pressure after initiation of therapy with enalapril. The possibility of hypotensive effects with enalapril can be minimized by either discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with enalapril. (See WARNINGS.)

Agents Causing Renin Release: The antihypertensive effect of VASOTEC® (Enalapril Maleate, MSD) is augmented by antihypertensive agents that cause renin release (e.g., diuretics).

Other Cardiovascular Agents: VASOTEC has been used concomitantly with beta adrenergic-blocking agents, methyldopa, nitrates, calcium-blocking agents, hydralazine, and prazosin without evidence of clinically significant adverse interactions.

Agents Increasing Serum Potassium: VASOTEC may attenuate potassium loss caused by thiazide-type diuretics. Potassium-sparing diuretics (e.g., spironolactone, triamterene, or amiloride), potassium supplements, or potassium containing salt substitutes may lead to significant increases in serum potassium. Therefore, if concomitant use of these agents is indicated, they should be used with caution and with frequent monitoring of serum potassium.

Pregnancy—Category C: There was no fetotoxicity or teratogenicity in rats treated with up to 200 mg/kg/day of enalapril (333 times the maximum human dose). Fetotoxicity, expressed as a decrease in average fetal weight, occurred in rats given 1200 mg/kg/day of enalapril, but did not occur when these animals were supplemented with saline. Enalapril was not teratogenic in rabbits. However, maternal and fetal toxicity occurred in some rabbits at doses of 1 mg/kg/day or more. Saline supplementation prevented the maternal and fetal toxicity seen at doses of 3 and 10 mg/kg/day, but not at 30 mg/kg/day (50 times the maximum human dose).

There are no adequate and well-controlled studies in pregnant women. VASOTEC should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether this drug is secreted in human milk. Because many drugs are secreted in human milk, caution should be exercised when VASOTEC is given to a nursing mother.

Pediatric Use: Safety and effectiveness in children have not been established.

Adverse Reactions: VASOTEC has been evaluated for safety in more than 10,000 patients, including over 1000 patients treated for one year or more. VASOTEC has been found to be generally well tolerated in controlled clinical trials involving 2677 patients.

The most frequent clinical adverse experiences in controlled trials were: headache (4.8%), dizziness (4.6%), and fatigue (2.8%). For the most part, adverse experiences were mild and transient in nature. Discontinuation of therapy was required in 6.0% of patients. In clinical trials, the overall frequency of adverse experiences was not related to total daily dosage within the range of 10 to 40 mg. The overall percentage of patients treated with VASOTEC reporting adverse experiences was comparable to placebo.

Other adverse experiences occurring in greater than 1% of patients treated with VASOTEC in controlled clinical trials were: diarrhea (1.6%), rash (1.5%), hypotension (1.4%), cough (1.3%), nausea (1.3%), and orthostatic effects (1.3%).

Clinical adverse experiences occurring in 0.5% to 1.0% of patients in the controlled trials included:

Cardiovascular: Syncope, orthostatic hypotension, palpitations, chest pain.

Nervous System: Insomnia, nervousness, paresthesia, somnolence.

Gastrointestinal System: Abdominal pain, vomiting, dyspepsia.

Other: Dyspnea, muscle cramps, hyperhydrosis, impotence, pruritus, asthenia.

Angioedema: Angioedema has been reported in patients receiving VASOTEC (0.2%). Angioedema associated with laryngeal edema and/or shock may be fatal. If angioedema of the face, tongue, or glottis occurs, treatment with VASOTEC should be discontinued and appropriate therapy instituted immediately. (See WARNINGS.)

Hypotension: Combining the results of clinical trials in patients with hypertension or congestive heart failure, hypotension (including postural hypotension and other orthostatic effects) was reported in 2.3% of patients following the initial dose of enalapril or during extended therapy. In the hypertensive patients, hypotension occurred in 0.9% and syncope occurred in 0.5% of patients. Hypotension or syncope was a cause for discontinuation of therapy in 0.1% of hypertensive patients. (See WARNINGS.)

Clinical Laboratory Test Findings:

Hyperkalemia: (See PRECAUTIONS.)

Creatinine, Blood Urea Nitrogen: Minor increases in blood urea nitrogen and serum creatinine, reversible upon discontinuation of therapy, were observed in about 0.2% of patients with essential hypertension treated with VASOTEC alone. Increases are more likely to occur in patients receiving concomitant diuretics or in patients with renal artery stenosis. (See PRECAUTIONS.)

Hemoglobin and Hematocrit: Small decreases in hemoglobin and hematocrit (mean decreases of approximately 0.3 g% and 1.0 vol%, respectively) occur frequently in hypertensive patients treated with VASOTEC but are rarely of clinical importance unless another cause of anemia coexists. In clinical trials, less than 0.1% of patients discontinued therapy due to anemia.

Other (Causal Relationship Unknown): Rarely, elevations of liver enzymes and/or serum bilirubin have occurred.

In overseas marketing experience, rare cases of neutropenia, thrombocytopenia, and bone marrow depression have been reported.

For more detailed information, consult your MSD representative or see Prescribing Information. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point. PA 19486.



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^{*}These rates include dues and assessments for a CAP/MPT member with 50 or more months of membership or retroactive coverage (matured rate). CAP/MPT offers coverage limits of \$1 million per occurrence with an aggregate of \$3 million per year.

CAP/MPT offers:

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WYOMING MEDICAL SOCIETY

JANUARY 30-31, 1987 • HOLIDAY INN • CODY, WYOMING

1987 WINTER SEMINAR

FRIDAY, JANUARY 30, 1987

8:45- 9:00 AM LEE K. HERMANN, MD Introduction

9:00- 9:45 AM VERN LAING, MD

Overview of Clinical Immunology

9:45-10:30 AM HENRY N. CLAMAN, MD Humoral (B-cell) Immunity; Physiology and Pathology

10:30-10:45 AM (Coffee Break)

10:45-11:30 AM HENRY N. CLAMAN, MD Cellular (T cell) Immunity; Physiology and Pathology

11:30-11:45 AM Question and Answer Period

11:45- 2:00 рм (Lunch)

2:00 PM LEE K. HERMANN, MD (Reconvene)

2:00- 2:45 PM PETER F. KOHLER, MD

Laboratory Evaluation of Patients with Immune Disorders

2:45- 3:30 PM VERN O. LAING, MD
Allergy (Atopy) with Emphasis on
Total and Specific IgE Levels in
Wyoming and Oklahoma Patients

3:30- 3:45 РМ (Coffee Break)

3:45- 4:30 PM PETER F. KOHLER, MD

Auto-immunity; Current Concepts
and Diseases

4:30- 4:45 PM LEE K. HERMANN, MD Question and Answer Period

SATURDAY, JANUARY 31, 1987

9:15 AM LEE K. HERMANN, MD (Reconvene)

9:15-10:00 AM DAVID L. COHEN, MD

AIDS I; Etiology, Epidemiology and
Public Health Aspects

10:00-10:45 AM DAVID L. COHEN, MD

AIDS II; Clinical Manifestations and
Therapy

10:45-11:00 AM (Coffee Break)

11:00-11:30 AM VERN LAING, MD MODERATOR Roundtable Discussion, Entire Faculty

11:45- 1:30 PM PRESENTATION OF SCIENTIFIC PAPERS BY WMS MEMBERS

FACULTY

Henry N. Claman, MD

Professor of Medicine
Chief, Division of Allergy
and Immunology
University of Colorado
Medical Center
Denver

David L. Cohen, MD

Assistant Professor of Medicine Division of Infectious Diseases University of Colorado Medical Center

Coordinator, AIDS Activities Denver Disease Control Center Denver General Hospital

Peter F. Kohler, MD

Professor of Medicine Tulane University Medical Center New Orleans Vern O. Laing, MD

Allergist Tulsa, Oklahoma



For Reservations and Information Contact: WYOMING MEDICAL SOCIETY P.O. Box 4009
Cheyenne, WY 82003-4009
Phone (307) 635-2424

BASF Group



AN OPEN LETTER TO CALIFORNIA PHYSICIANS

Vicodin is a Schedule III analgesic in California

Dear Doctor,

As a Schedule III drug, prescriptions for Vicodin may be:

- Refilled 5 times within 6 months.
- Telephoned into local pharmacies.
- Written on regular prescription pads. No triplicate pads are necessary.

We regret any inconvenience caused by the inadvertent reclassification of Vicodin in California to a Schedule II status during July and August of this year. This has been rectified by the California assembly.

Vicodin will continue to be sampled per your request. Thank you for your support of Vicodin.

Please continue to specify "Dispense as written" for the original hydrocodone analgesic.

Sincerely,

John La Lota Product Manager

Vicodin



Hydrocodone bitartrate 5 mg. (Warning: May be habit forming) with acetaminophen 500 mg.

Greater patient acceptance and longer lasting pain relief.

Please see accompanying brief summary.

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Hospital Medical Staff Section convesecond Annual Assembly and Medical Sconference			1
☐ Technical Exhibits by more than 125 of feature state-of-the-art medical equipm		formation	
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For complete program information and ar (415) 863-5522, ext. 404, or mail in the		orm call Barbara S	mart at
California Medical Association Attention: Barbara Smart P.O. Box 7690 San Francisco, CA 94120-7690	Na		
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PHYSICIANS WANTED

80-MEMBER MULTISPECIALTY GROUP seeking two Board certified or eligible Family Practice physicians for openings in satellite offices in Ceres and Patterson. Generous first year guarantee with incentives based on productivity. Excellent fringe benefits including malpractice, retirement, health/dental insurance. Located in Northern California within 2 hours of San Francisco, Yosemite, Sierra Mountains, Carmel. Send CV with references to: C. R. Maino, MD, Gould Medical Foundation, 600 Coffee Road, Modesto, CA 95355.

ARIZONA BASED PHYSICIAN RECRUITMENT firm has opportunities Coast to Coast. "Professionals working with Professionals." Over 14 years experience. Call (602) 795-7474; or send CV to: Mitchell & Associates, Inc., 2761 N. Country Club Rd., Ste. 202, Tucson, AZ 85716.

OBSTETRICS AND GYNECOLOGY—multispecialty, family care oriented group has two excellent practice opportunities for OB/GYN specialists. We are located in a growing, dynamic Southwest city and offer an excellent benefit and incentive salary program. Send CV to D. R. Molesworth, Administrator, The Tucson Clinic, P.C., PO Box 26926, Tucson, AZ 85726.

MD NEEDS—SOUTHERN CALIFORNIA ON-LY—FPS, GP, IM, OB/GYN, OR and other subspecialties needed for private groups and associations. Baker, Ellerd and Associates, Inc., 16200 Ventura Blyd., Ste. 426, Encino, CA 91436; call (818) 995-4311.

EMERGENCY MEDICINE Career opportunities for primary care physicians are immediately available with Spectrum throughout Arizona. Openings are for emergency department medical directors and full-time staff physicians at select client hospitals in Arizona. You can choose the location and practice situation that meets your needs. Guaranteed competitive rate of compensation, full protection of occurrence malpractice insurance coverage, plus Medical Directors receive paid life, health, disability and dental insurance which includes dependents. For more details on these excellent opportunities in Arizona, contact Bill Salmo, Spectrum Emergency Care, 6275 Lehman Dr., Ste. C202, Colorado Springs, CO 80918; 1 (800) 525-3681; (303) 590-1755.

FAMILY PRACTICE—Multispecialty family care oriented group needs additional Family Practice Physicians. Excellent practice opportunity in a dynamic Southwest city; good benefits and salary plan. Send CV to: D. R. Molesworth, Administrator, The Tucson Clinic, P.C., PO Box 26926, Tucson, AZ 85726.

PHYSICIANS WANTED

INTERNAL MEDICINE—Multispecialty group needs additional Internists. A growing group in a dynamic Southwest community; excellent practice; benefits; and investment opportunities. Send CV to: D. R. Molesworth, Administrator, The Tucson Clinic, P.C., PO Box 26926, Tucson, AZ 85726.

VANCOUVER/CAMAS, WASHINGTON. BC/BE Family Practitioner to join a growing FP department within a well established 30-physician multispecialty group. Satellite clinic is in a high growth area with a multitude of outstanding recreational, cultural and educational opportunities in nearby Portland, Oregon, Mt. Hood, and the Columbia Gorge. High quality practice with excellent vacation and benefits package. Salary first two years, with potential for full partnership. Send CV to: Roger R. Garretson, 700 N.E. 87th Ave., Vancouver, WA 98664.

IMMEDIATE OPENING—Immediate Care Center. Large, multispecialty clinic located in southeastern Washington has an opening for a qualified physician to join a Board certified Emergency Physician in staffing a walk in/immediate care center. Corporate paid retirement plan, excellent compensation package, superior recreational and cultural opportunities in a family-oriented environment. Send complete CV to James Mercer, MD, Walla Walla Clinic, 55 W. Tietan, Walla Walla, WA 99362; or call 1-(509) 522-0550.

ALLERGIST/CLINICAL IMMUNOLOGIST (Pediatric and Adult) BE/BC to join a well established allergist working in an 80 plus physician multispecialty group located in California's Central Valley. Within two hours of San Francisco, Yosemite, Carmel and the Sierras. Generous guaranteed base salary with incentive, early partnership. Reply with CV and references to: C. R. Maino, MD, Gould Medical Foundation, 600 Coffee Rd., Modesto, CA 95355

OTOLARYNGOLOGIST. Position available with 35-member multispecialty group; BC/BE; immediate opening; full range of benefits plus immediate shareholder status; excellent opportunity; central coast of California. Respond with CV to: Colin J. Wells, MD, San Luis Medical Clinic, Ltd., 1235 Osos St., San Luis Obispo, CA 93401-3619. No phone calls please.

CALIFORNIA. BC/BE Pediatrician and Internist to join young group at the edge of the Sierras. Send CV to Number 149, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

PHYSICIANS WANTED

BUSY FEMALE GYN looking for quality associate. Excellent opportunity in suburban Los Angeles for BC/BE OB/GYN. Full- or part-time. Gynecology only, but great potential for full Obstetrics practice if desired. Position available immediately. Must be sensitive, well-trained, personable, and hardworking man or woman. Please reply to Number 152, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

INTERNIST BC/BE—Opening for General Internist in a 32-physician, multispecialty group located in the Pacific Northwest. Guaranteed salary and immediate full participation in incentive program, plus outstanding benefit package. Please submit your CV to the Search Committee, Walla Walla Clinic, 55 W. Tietan, Walla Walla, WA 99362.

OREGON—Opportunity for a committed, energetic physician to become a leader in the development of a primary care group practice in Portland, Oregon. Affiliated with a prominent medical center, the practice will open multiple offices offering care which reflects the traditional values of the profession in a competitive manner. Salaried position with bonus, stock options, and excellent benefits. Send CV to: Number 154, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

PEDIATRICIAN: The San Luis Medical Clinic, Ltd. a 35-member multispecialty group practicing on the California central coast has an immediate need for a general Pediatrician. Full range of benefits and all practice costs paid. Send CV to: Colin J. Wells, MD, San Luis Medical Clinic Ltd., 1235 Osos St., San Luis Obispo, CA 93401-3619. No telephone calls please.

MINNEAPOLIS—Family Practice, Internal Medicine, Cardiology, Child Psychiatry, Adult Psychiatry, Obstetrics/Gynecology, Ophthalmology. Join established group in one of America's leading metropolitan areas. Group provides professional liability, four weeks vacation, two weeks conference leave, disability, retirement, hospital dues and more. Must be Board certified or Board eligible. Direct inquiries to: Paul J. Brat, MD, Medical Director, Group Health, Inc., 2829 University Ave. SE, Minneapolis, MN 55414.

ARIZONA—VA Medical Center, Prescott, Arizona, Medical Service is recruiting for a full-time, Board certified Geriatrician and/or General Internist. Position available now. Prescott is a 217 bed general medical hospital with an active medical service, ICU/CCU, Ambulatory Care, Rehabilitation Medicine Service, Alcohol Dependency Treatment Program, and intermediate bed care units. Prescott is located in the mountains of North Central Arizona with a population of 25,000. Salary range is \$70,000 to \$80,000 depending on qualifications. Send curriculum vitae to: F. C. Lepperd, Jr., MD, Chief of Staff, VA Medical Center, Prescott, AZ 86313; or call (602) 445-4860, Ext. 301; Equal Opportunity Employer.

FIRCREST SCHOOL for the developmentally disabled seeks Pediatrician/chronic care. Interdisciplinary team setting. University affiliation encouraged. Submit résumé to R. Doan, MD, Fircrest School, 15230-15th NE, Seattle, WA 98155. Apply Fircrest Personnel, (206) 364-0300, ext. 430, EOE.

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Well-established and successful HMO is seeking Specialists and Primary Care physicians for our facilities in Los Angeles and Orange Counties. Located in close proximity to major teaching centers, we offer the opportunity for continued professional development and rewarding clinical practice. Excellent compensation and benefits package, including profit sharing. Please send CV to:

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(Continued on Page 734)

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WESTERN STATES OPENINGS

Several multispecialty groups and hospitals have asked us to recruit for over 200 positions of various specialties.

Western States Physician Services 240 W. Shaw, Suite C Clovis, CA 93612 (209) 297-7748

FAMILY OR EMERGENCY MEDICINE physician for Industrial clinic treating urban port workers in Washington. Establish primary contact with area industries. Satellite of multispecialty clinic. No nights or weekends. Salary and excellent benefits. Send curriculum vitae or call: The Friedrich Group, Inc., 9284 Ferncliff NE, Bainbridge Island, WA 98110; (206) 527-3141 or (206) 842-5248.

FAMILY PRACTICE. Position available with 35-member multispecialty group; BC/BE; immediate opening; full range of benefits plus immediate shareholder status; excellent opportunity; central coast of California. Respond with CV to: Colin J. Wells, MD, San Luis Medical Clinic, Ltd., 1235 Osos St., San Luis Obispo, CA 93401-3619. No phone calls please.

NEW MEXICO—Primary Care Physician for 600-bed psychiatric/geriatric hospital in Las Vegas, New Mexico. Competitive salaries and generous benefits including on-call compensation. Superb climate and nearby recreational facilities. Contact: Medical Director, Las Vegas Medical Center, PO Box 1388, Las Vegas, NM 87701-1388 or call (505) 425-6711, ext. 5402.

ADDITIONAL INTERNIST NEEDED for busy 5 physician multispecialty group. Beautiful, well equipped 6 year old office just 75 feet from 34 bed hospital with ICU/CCU unit. This all Board certified group consists of 3 Family Practitioners, 2 General Surgeons, and 1 Internist. Coastal retirement town offers top notch school system and excellent array of activities. Located just 75 easy miles from Portland adds even more cultural and shopping opportunities. For further information contact Rick Bigger days at (503) 738-9551.

OB/GYN position available with 35-member multispecialty group; BC/BE; immediate opening; full range of benefits plus immediate shareholder status; excellent opportunity; central coast of California. Respond with CV to: Colin J. Wells, MD, San Luis Medical Clinic, Ltd., 1235 Osos St., San Luis Obispo, CA 93401-3619. No phone calls please.

CHIEF OF INTERNAL MEDICINE (Physician III)—\$6,151-\$6,504/monthly. Applications are being accepted for the Chief of Internal Medicine with the County Hospital. Natividad Medical Center is a 204-bed teaching hospital affiliated with the University of California, San Francisco for a family practice residency program. Excellence in teaching and administrative experience required along with Board certification. For applications and further information, submit CV to Ray K. Bolinger, Hospital Administrator, Natividad Medical Center, PO Box 8-1611, Salinas, CA 93912-1611; or phone (408) 757-0585. FFD until sufficient applications are received.

B/C-B/E DIAGNOSTIC RADIOLOGIST

Hospital and office practice. All modalities except MRI. Hands on experience in real time ultrasound desired. Excellent salary and benefits, commensurate with experience. Early partnership. Will consider locums. Send CV to Radiology, 5581 N. Fresno St., Fresno, CA 93710; (209)439-2464.

FAMILY PRACTICE OPPORTUNITY. Five person Portland, Oregon, group looking for two new partners. Solid growing practice with HMO and PPO affiliations. First year guarantee plus benefits. Contact: The Friedrich Group, Inc., 9284 Ferncliff NE, Bainbridge Island, WA 98110; (206) 527-3141 or (206) 842-5248.

POSITIONS AVAILABLE

MEDICAL DIRECTOR—Annual salary established to \$103,000. Excellent fringe benefits/continuing education program/self-insured. The Los Angeles Department of Water and Power (DWP) is seeking a California licensed MD with increasingly responsible professional and administrative experience in occupational health programs for employment as Medical Director. DWP has over 10,000 employees and an expanding medical program providing entry physicals; medical and minor surgical services; medical consultation on occupational health issues, including Workers' Compensation and OSHA Medical Surveillance through the use of mobile medical vans at statewide DWP facilities. Please submit a résumé, by November 25, 1986 to Mr Jeff Pfau, Manager of Occupational Health and Benefits, Department of Water and Power, 111 N. Hope St., Room 549, Los Angeles, CA 90012. Your résumé, clearly delineating your relevant experience and training, will be accepted in confidence. Questions? Telephone Mr Pfau at (213) 481-4575. The Department of Water and Power is an Equal Opportunity Affirmative Action Employer.

SAN DIEGO

Busy, multispecialty group in San Diego is expanding and will be adding Specialists and Family Physicians to its staff. Outstanding practice opportunities in an ideal geographic setting. For immediate consideration, please send CV to: Mirriam Stephens, Director of Professional Recruitment, SMITH HANNA Medical Group, 5703 Oberlin Dr., Ste. 302-49, San Diego, CA 92121

GENERAL INTERNAL MEDICINE with an emphasis on Cardiology. Private multispecialty clinic in prime urban location in Washington. First year salary guarantee plus incentives and excellent benefits including Pacific Northwest life-style. Contact: The Friedrich Group, Inc., 9284 Ferncliff NE, Bainbridge Island, WA 98110; (206) 527-3141 or (206) 842-5248.

NORTHERN CALIFORNIA, EMERGENCY MEDICINE. Full-time positions available in the Emergency Room at The University of California Davis Medical Center. The University serves a large region of Northern California and is a major trauma center. Emergency physicians teach and supervise medical students and housestaff in addition to treating patients, primarily. Opportunities exist for involvement in other School of Medicine teaching activities. Applicants should send curriculum vitae to Robert W. Derlet, MD, University of California Davis Medical Center, 2315 Stockton Blvd., Department of Emergency Medicine, Trailer 1219, Sacramento, CA 95817.

PRIVATE/NON-PROFIT MULTISPECIALTY GROUP in Hispanic community seeks Board eligible/Board certified Internist, Family Practitioner and Pediatrician to join established group to provide comprehensive ambulatory and in-patient care. Send curriculum vitae to: Community Health Foundation, 3945 E. Whittier Blvd., Los Angeles, CA 90023; (213) 266-4690, Ext. 250—Personnel.

SAN FRANCISCO—ONE HOUR. Multispecialty group which is growing fast is accepting applications for the following specialties: Pediatrician, Pulmonologist, Surgeon, ENT. First year includes salary plus benefits. After one year partnership may be offered. Reply to Number 157, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

FAMILY PRACTITIONER to join established 42year-old Family Practitioner in Garden Grove, California. Part-time to start. Salary guarantee to percentage after one year. Send CV to Number 158, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

TALENTED INTERNIST full-time in private practice with four other Internists covering rural ER/Acute medicine. Involves four two night shifts per month. Scheduling flexible. Sense of humor preferred. 60K. C. Rath, MD, 199 E. Webster St., Colusa, CA 95932; (916) 458-7739.

PHYSICIANS WANTED

PHYSICIAN POSITIONS: Multi-site primary care non-profit corporation is seeking physicians for full-or part-time practice. General Practice, Family Practice, Internal Medicine physicians needed. Competitive salary and excellent benefit package. All inquiries strictly confidential. Contact Jack Hicks, Assistant Director, at (805) 845-3731 for more information or send CV to Clinica Sierra Vista, PO Box 457, Lamont, CA 93241.

PATHOLOGIST: Large pathology group in greater Los Angeles area seeking qualified Anatomic and Clinical Pathologist. Prefer applicants with fellowship training or 1-2 years experience. Excellent position with growth potential. Send résumé to: Glenview Pathology Medical Group, 9331 Venice Blvd., Culver City, CA 90230, Attn: Dr Emanuel Abrams.

FAMILY PRACTICE PHYSICIAN/MEDICAL DI-RECTOR. (Scenic Northwest) Two positions available: Family Practice Physician and Physician/ Medical Director. Must be Family Practice physician BC/BE. System of four primary care community clinics. Full-scope family practice, hospital and SIF privileges. New facilities, excellent salary and fringes. Send résumé to: Community Health Care Delivery Systems FC-3312, 3629 South D St., Tacoma, WA 98408. EOE.

PUGET SOUND/WASHINGTON. Pediatrician sought for busy multispecialty urban group practice near children's hospital. Current experience in Pediatrics and newborn intensive care needed. Competitive income and benefit package. Send CV or call: The Friedrich Group, Inc., 9284 Ferncliff NE, Bainbridge Island, WA 98110; (206) 842-5248 or (206) 527-3141.

EPIDEMIOLOGICAL HEALTH ANALYZER—Minimum one year experience with BS degree either field of epidemiology, health, parasitology or related field to assist this medical group in investigating various types of epidemic contagious diseases prevalent within Southern California. Will analyze such information as how many persons in certain areas were affected, how rapid a spread, localities where the diseases became a sudden prevalence, etc. Salary \$28,200 per year. Send ré sumé to: Westmoreland Medical Group, 3030 W. 6th St., Los Angeles, CA 90020; Attn: Dr Song.

FAMILY PHYSICIAN, BC or BE, residency-trained, to join two very busy young FP's in Phoenix, Arizona, July 1987. No OB. Excellent income. Great city. 310 days of sunshine. Contact G. A. Rada, MD, 12251 N. 32nd St., Ste. 4, Phoenix, AZ 85032; (602) 992-1900.

HAWAII. ER PHYSICIAN NEEDED. Full-time, permanent, career position on Kauai. Part of 36-physician multispecialty group. Salary \$50-\$70K, plus vacation, CME, and complete benefit package. 1,000 visits/month. Full stockholder in 1-2 years. Six ER physicians share shifts evenly. Surfing, diving, fishing, hunting, rodeo, sailing, windsurfing, dirt-biking and polo. Tail covered 100% at end of 5 years. This is a peach, don't hesitate. (Board eligible strongly preferred.) Please submit CV to: James Scamahorn, MD, Kauai Medical Group, 3420-B Kuhio Highway, Lihue, HI 96766. Phone: (808) 245-1012.

PHYSICIANS WANTED. Physicians, BC/BE needed immediately to join expanding multispecialty group. Practice in rapidly growing Southwest community (population 500,000+). Fee-for-service and prepaid health care. Group includes Family Practice/Pediatrics, Internal Medicine/Subspecialties/24 hour Urgent Care. Teaching appointment. Position offers excellent compensation and benefits plus full pension and profit sharing. Relocation expenses. Interested individuals should reply with curriculum vitae to: Southwest Medical Associates, 333 N. Rancho Dr., Ste. 100, Las Vegas, NV 89106.

PHYSICIANS WANTED

SAN FRANCISCO—1 year Fellowship in Psychosomatic Medicine and Consultation Liaison Psychiatry offered by St. Mary's Medical Center, a 550 bed private teaching hospital. Supervised clinical, teaching, and administrative experience in unique Med-Psych inpt unit, Med-Surg wards, Psychiatry and Medicine Clinics, and Sleep Disorders Center. Board eligibility in Psychiatry, Neurology or Medicine required. Contact: D. Nevins, MD, St. Mary's Medical Center, 450 Stanyan St., San Francisco, CA 94117.

SAN FRANCISCO, EMERGENCY MEDICINE. Part-time and full-time positions available in busy emergency department (32,000 patient visits/year) in full service hospital with excellent in-house specialty back-up. Prefere ABEM or ABIM certified/ eligible, experienced Emergency Physician. Competitive salary, excellent benefits. Call or write Pat Salber, MD, Kaiser Permanente Medical Group, 2200 O'Farrell St., San Francisco, CA 94115; (415) 929-4020.

PHYSICIAN, full-time, fee-for-service, Pacific Bell Medical Program. Will require assignments in San Ramon or San Jose area. Send CV to Martha Balabegians, MD, 2600 Camino Ramon, Room 1W001, San Ramon, CA 94583.

PACIFIC NORTHWEST. Practice high-risk Obstetrics using latest technology as part of a leading multispecialty clinic. Enjoy Pacific Northwest life-style. Prime urban location. Malpractice coverage provided. Salary guarantee. Contact: Sandra Jones, The Friedrich Group, Inc., 9284 Ferncliff NE, Bainbridge Island, WA 98110; (206) 527-3141 or (206) 842-5248.

CALIFORNIA: Openings for emergency department Medical Directors and full-time staff physicians are immediately available at two client hospitals in California. Guaranteed rate of compensation, occurrence malpractice insurance coverage, flexible scheduling, CME allowance, plus more. For additional details contact Bill Salmo, Spectrum Emergency Care, 6275 Lehman Dr., Ste. C202, Colorado Springs, CO 80918; 1 (800) 525-3681; (303) 590-1755.

MEDICAL DIRECTOR OF ADOLESCENT CHEMICAL DEPENDENCY PROGRAM—Marshal Hale Memorial Hospital currently seeks a physician (background in internal medicine or general practice preferred) to provide medical leadership, evaluation and patient care for our 20-bed unit. Successful applicant should have experience in the treatment of chemical dependency and/or experience with adolescents. Please send résumé to: Nicholas Talone, Vice President, Professional Services, Marshal Hale Memorial Hospital, 3773 Sacramento St., San Francisco, CA 94118; (415) 666-7837.

GASTROENTEROLOGIST—BC/BE for multispecialty group downtown San Francisco. Send CV and references to: 757 Sutter Medical Clinic, Ste. 100, San Francisco, CA 94109.

ACADEMIC EMERGENCY MEDICINE-The University of California, Davis, School of Medicine is recruiting for a full-time faculty position at the Assistant or Associate Professor level to serve in the Division of Emergency Medicine and Clinical Toxicology. The UCD Emergency Department provides comprehensive emergency care and is a major trauma center. Candidates must be Board certified in Emergency Medicine or Internal Medicine with experience in emergency medicine, and be eligible for licensure in California. The candidate must have prior academic and clinical experience in emergency medicine. Experience in clinical toxicology is highly desirable. A letter outlining research, teaching background and interests, experience, a curriculum vitae and the names of five references must be received by February 28, 1987. Reply to: Robert W. Derlet, MD, Chair of Emergency Medicine Search Committee, Department of Internal Medicine, University of California, Davis, Medical Center, 2315 Stockton Blvd., Sacramento, CA 95817. The University of California is an Affirmative Action/Equal Opportunity Employer.

PHYSICIANS WANTED

URGENT CARE CENTER. Arizona, Phoenix and Tucson areas. Opportunity for physician with Family Practice or IM background in hospital-affiliated urgent care centers. Please send CV to: Executive Director—Urgent Care, Mercy Services Corporation-Phoenix, 350 W. Thomas Rd., Phoenix, AZ 85013.

LOCUM TENENS

LOCUM TENENS SERVICE WESTERN PHYSICIANS REGISTRY

offers coverage for vacation or continuing education. To arrange coverage for your practice or to participate as temporary physician, contact: Carol Sweig, Director, 1315 Evans Avenue, San Francisco, CA 94124; (415) 826-7676.

SITUATIONS WANTED

BOARD CERTIFIED INTERNIST completing two year Fellowship in Critical Care Medicine. Competent in all ICU procedures. Looking for position as Intensivist in medical or med./surg. ICU in California, Arizona, Oregon or Colorado. Available July 1987. Please reply to Number 156, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

PEDIATRICIANS—Husband and wife, are looking for 1 or 2 positions starting August 1987. Prefer Northern California but considering all options. Write Number 159, Western Journal of Medicine. PO Box 7602, San Francisco, CA 94120-7602.

GENERAL VASCULAR SURGEON, certified ABS, GVS; FACS, California licensed. Seeking association at least 80% peripheral vascular. Will consider multispecialty group. Reply Number 160, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

SEMINARS

THE AMERICAN ASSOCIATION OF ORTHO-PAEDIC MEDICINE presents "Diagnostic Models of Musculoskeletal Pain," May 12-17, 1987, Montreal, Canada. Contact: Deborah Staller, Exec. Sec., AAOM, 926 E. McDowell Rd., Ste 202, Phoenix, AZ 85006; (602) 254-5315.

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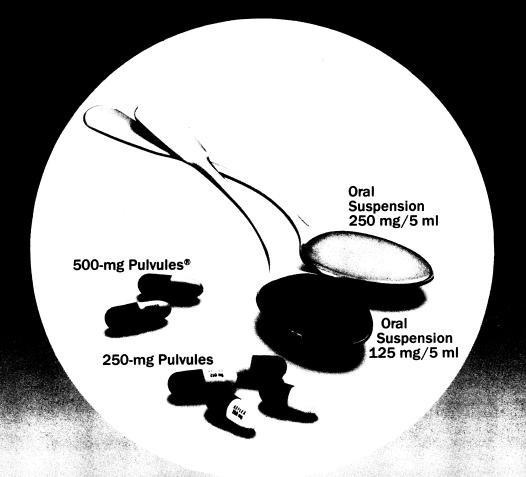
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References: 1. Data on file, Hoffmann-La Roche Inc., Nutley, NJ. 2. Feighner JP, et al: Psychopharmacology 61:217-225, Mar 22, 1979.



A brighter perspective...sooner

Limbitrol® @ Tranquilizer—Antidepressant

Before prescribing, please consult complete product information, a summary of which follows: Indications: Relief of moderate to severe depression associated with moderate to severe anxiety. Contraindications: Known hypersensitivity to benzodiazepines or tricyclic antidepressants. Do not use with monoamine oxidase (MAO) inhibitors or within 14 days following discontinuation of MAO inhibitors since hyperpyretic crises, severe convulsions and deaths have occurred with concomitont use; then initiate cautiously, gradually increasing dosage until optimal response is achieved. Contraindicated during acute recovery phase following myocardial infarction.

Warnings: Use with great care in patients with history of urinary retention or angle-closure glau-

coma. Severe constitution may occur in patients taking tricyclic antidepressants and anticholin-ergic-type drugs. Closely supervise cardiovascular patients. (Arrhythmias, sinus tachycardia and prolongation of conduction time reported with use of tricyclic antidepressants, especially high doses. Myocardial infarction and stroke reported with use of this class of drugs.) Caution patients about possible combined effects with alcohol and other CNS depressants and against hazardous

occupations requiring complete mental alertness (e.g., operating machinery, driving).

Usage in Pregnancy: Use of minor tranquilizers during the first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Since physical and psychological dependence to chlordiazepoxide have been reported rarely, use

caution in administering Limbitrol to addiction-prone individuals or those who might increase dosage; withdrawal symptoms following discontinuation of either component alone have been reported (nausea, headache and malaise for amitriptyline; symptoms [including convulsions] similar to those of barbiturate withdrawal for chlordiazepoxide).

Precautions: Use with caution in patients with a history of seizures, in hyperthyroid patients or those on thyroid medication, and in patients with impaired renal or hepatic function. Because of the possibility of suicide in depressed patients, do not permit easy access to large quantities in these patients. Periodic liver function tests and blood counts are recommended during prolonged treatment. Amitriptyline component may block action of guanethidine or similar antihypertensives. When tricyclic antidepressants are used concomitantly with cimetidine (Tagamet), clinically signifwhen incyclic deniberlessants are used controlling with controlling the contro oversedation, confusion or anticholinergic effects.

Adverse Reactions: Most frequently reported are those associated with either component alone.

drowsiness, dry mouth, constipation, blurred vision, dizziness and bloating. Less frequently occurring reactions include vivid dreams, impotence, tremor, confusion and nosal congestion.

Many depressive symptoms including anorexia, fatigue, weakness, restlessness and lethargy have been reported as side effects of both Limbitrol and amitriptyline. Granulocytopenia, jaundice and hepatic dysfunction have been observed rarely.

The following list includes adverse reactions not reported with Limbitrol but requiring consideration because they have been reported with one or both components or closely related drugs: Cardiovascular: Hypotension, hypertension, tachycardia, palpitations, myocardial infarction arrhythmias, heart block, stroke.

Psychiatric: Euphoria, apprehension, poor concentration, delusions, hallucinations, hypomania and increased or decreased libido

Neurologic: Incoordination, ataxia, numbness, tingling and paresthesias of the extremities, extra-pyramidal symptoms, syncope, changes in EEG patterns.

Anticholinergic: Disturbance of accommodation, paralytic ileus, urinary retention, dilatation of

Alleraic: Skin rash, urticaria, photosensitization, edema of face and tongue, pruritus Hematologic: Bone marrow depression including agranulocytosis, eosinophilia, purpura, thrombocytopenia

Gastrointestinal: Nausea, epigastric distress, vomiting, anorexia, stomatitis, peculiar taste, dianthea, black tonque.

Endocrine: Testicular swelling and gynecomastia in the male, breast enlargement, galactorrhea and minor menstrual irregularities in the female, elevation and lowering of blood sugar levels, and syndrome of inappropriate ADH (antidiuretic hormone) secretion.

Other: Headache, weight gain or loss, increased perspiration, urinary frequency, mydriasis, jaundice, alopecia, parotid swelling.

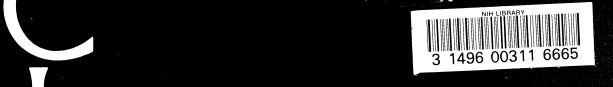
Overdosage: Immediately hospitalize patient suspected of having taken an overdose. Treatment is symptomatic and supportive. I.V. administration of 1 to 3 mg physostigmine salicytate has been reported to reverse the symptoms of amitriptyline poisoning. See complete product information for manifestation and treatment

Dosage: Individualize according to symptom severity and patient response. Reduce to smaller effective dosage when satisfactory response is obtained. Larger portion of daily dose may be taken at bedtime. Single h.s. dose may suffice for some patients. Lower dosages are recommended for the elderly.

Limbitrol DS (double strength) Tablets, initial dosage of three or four tablets daily in divided doses increased up to six tablets or decreased to two tablets daily as required. Limbitrol Tablets, initial increased up to six dubies of decreased in who dubies, starting a request. Elimination decrease, decreased the decreased in the decrease decrease. How Supplied: Double strength (DS) Tablets, white, film-coated, each containing 10 mg chlor-diazepoxide and 25 mg amilitiptyline (as the hydrochloride salt), and Tablets, blue, film-coated, each containing 5 mg chlordiazepoxide and 12.5 mg amilitiptyline (as the hydrochloride salt). Available in bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 50.







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